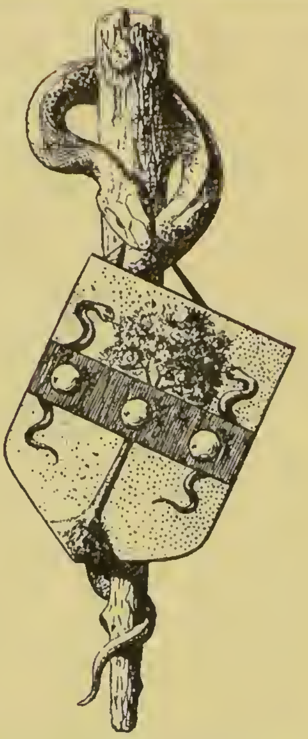


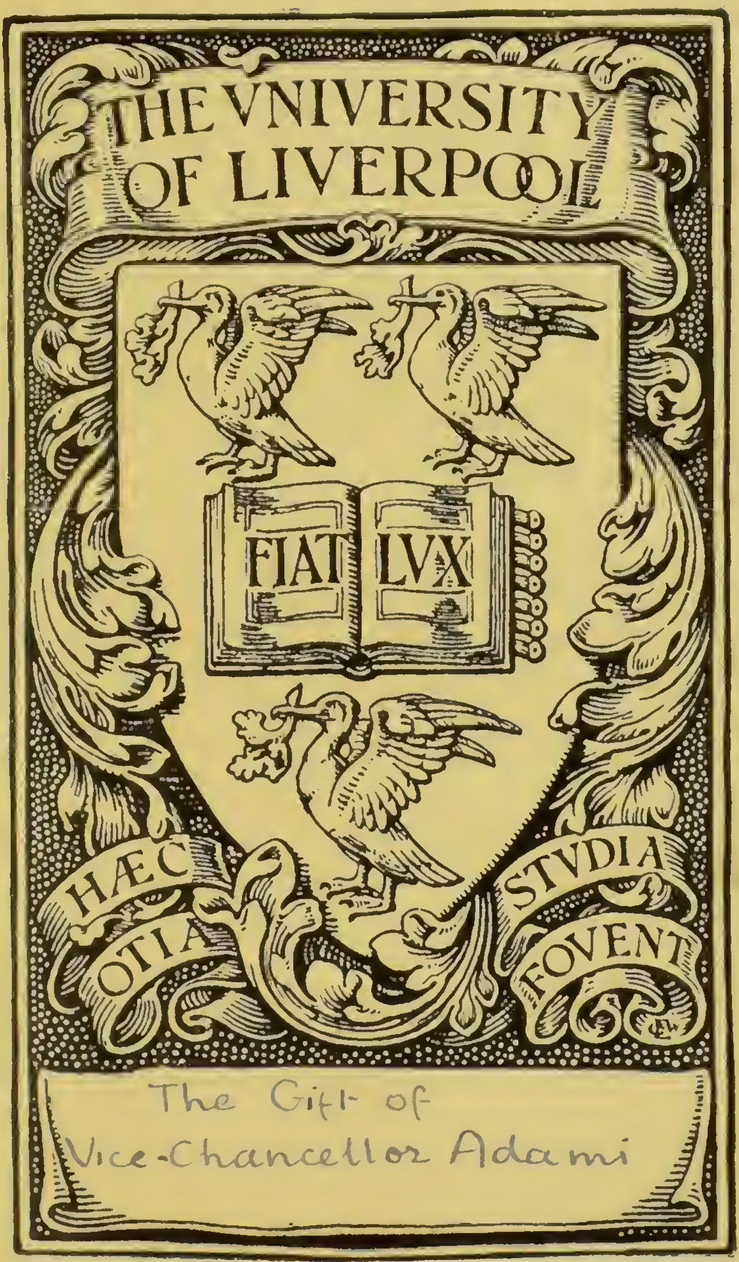
J.GEORGE ADAMI

Ipse inv et del MCMX

DISPOSED OF AS DUPLICATES
BY THE UNIVERSITY LIBRARY

22102064109

Med
K17917



The Gift of
Vice-Chancellor Adami

DISPOSED OF AS DUPLICATES
BY THE UNIVERSITY LIBRARY

Digitized by the Internet Archive
in 2016

https://archive.org/details/b2813901x

TRANSACTIONS OF THE

SECTION ON
PATHOLOGY AND PHYSIOLOGY

of the
American Medical Association
at the Fifty-fourth Annual
Session, held at New Orleans,
May 5 to 8, 1903 :: :: :: :: ::

CHICAGO:
PRESS OF AMERICAN MEDICAL ASSOCIATION
ONE HUNDRED AND THREE DEARBORN AVENUE
1904

WELLCOME INSTITUTE
LIBRARY
Coll. welMOmec
Call
No. QV

OFFICERS FOR 1902-1903

CHAIRMAN.

VICTOR C. VAUGHAN - - - - ANN ARBOR, MICH.

SECRETARY.

JOSEPH McFARLAND - - - - PHILADELPHIA.

EXECUTIVE COMMITTEE.

W. S. HALL, CHICAGO.
L. HEKTOEN, CHICAGO.
FRANK B. WYNN, INDIANAPOLIS.

OFFICERS FOR 1903-1904

CHAIRMAN.

JOSEPH McFARLAND - - - - - PHILADELPHIA.

SECRETARY.

HENRY A. CHRISTIAN - - - - - - BOSTON.

EXECUTIVE COMMITTEE.

L. HEKTOEN, CHICAGO.
FRANK B. WYNN, INDIANAPOLIS.
VICTOR C. VAUGHAN, ANN ARBOR, MICH.

CONTENTS

PAGE.

Officers 5

Multiple Periosteal Sarcomata of the Cranium, with Involvement of Retroperitoneal Lymph Nodes, and Attending Severe, Probably Pernicious, Anemia. Walter L. Bierring 9

The Apparent Immunizing Value of Attenuated Tubercle Bacilli. E. A. de Schweinitz 17

Experiments with Rennet and Antirenene. Joseph McFarland 24

The Protoplasmic Activity of the Renal Epithelium, as Determined by the Elimination of Pigments Injected into the Circulation. William S. Carter 35

The Influence of Consanguinity on the Organs of Special Sense. Lee W. Dean 51

Precision in the Determination of Human Parasites. Henry B. Ward 58

Condition of the Endothelium in Cases of Uterine Myomata. Thomas S. Cullen 77

A Case of Aerogenes Capsulatus Infection of the Neck. Louis Leroy 79

Neuroglia Tissue and Ependymal Epithelium in Teratoid Tumors. Henry A. Christian 87

The Morphology and Biology of the Parasites from a Case of Systemic Blastomycosis. F. J. Otis and Newton Evans 110

Uncinariasis in the South. Further Observation. Claude A. Smith 135

The Capacity of a Human Muscle for Work. Jesse George Holmes 150

New Physiologic Apparatus. The Frog-board Myograph and the Manometer Tambour. Winfield S. Hall 167

Report on the Scientific Exhibit of the American Medical Association, at New Orleans, May 5-8, 1903 174

Executive Session 188

Index 191

MULTIPLE PERIOSTEAL SARCOMATA OF THE CRANIUM,

WITH INVOLVEMENT OF RETROPERITONEAL LYMPH NODES, AND ATTENDING SEVERE, PROBABLY PERNICIOUS, ANEMIA.

WALTER L. BIERRING, M.D.
Professor of Theory and Practice of Medicine and Clinical Medicine,
University of Iowa.
IOWA CITY, IOWA.

Through the exhaustive work of Warthin the retroperitoneal lymph nodes or hemolymph glands have been given an important rôle in human pathology. Changes in these hitherto frequently unrecognized structures are specially significant of anemia and processes accompanied by hemolysis.

I feel that the case, a description of which I wish to submit, illustrates this relationship in a special way, and offers a few additional points of pathologic interest as to warrant its being presented before this section.

The case occurred in the practice of Dr. C. B. Kimball of West Liberty, Iowa, to whom I feel indebted for calling my attention to it and furnishing me with the principal clinical data, which in brief were as follows:

A. B., girl 5 years of age, who until three months before her death enjoyed good health and had been regarded as an unusually robust child. When first seen by her medical attendant she presented a mild degree of anemia, a slight rise of body temperature, some malaise, impairment of appetite, and physical weakness. During the period of illness mentioned, the anemia assumed a progressive pernicious character, the pyrexia of one to two degrees continued, and the emaciation and physical weakness proportionately increased.

At my first opportunity to see the case, Oct. 5, 1902, the anemia was quite pronounced and the child appeared weak and listless. There was no enlargement of any of the palpable lymph nodes, but over the frontal region a soft subcutaneous sessile tumor-like enlargement, about three centimeters in diameter, was observed, which was apparently attached to the frontal bone.

A hemic murmur was noted over the base of the heart; the lungs were negative; the splenic area of dulness not increased, and the organ not palpable. Area of hepatic dullness not increased, Urine acid, specific gravity 1,022; chemical tests negative. Signs of intracranial pressure were not present.

I saw her again one week before her death, when she appeared in a semicomatose state, the anemia being very profound and emaciation specially marked. There was no noticeable change in the different lymph nodes. The spleen was not enlarged, though a perceptible yet slight enlargement was noted in the hepatic area of dullness. Urine negative. Lungs negative. Hemic murmur still very pronounced over the basal region of the heart.

The frontal tumor had apparently enlarged and four more tumors were now to be detected over the parietal and occipital bones, and one over the left mastoid region. A slight degree of exophthalmus was present. The blood count revealed erythrocytes, 982,000; leucocytes, 9,600; hemoglobin, 30 per cent. Differential count in 17,874 red cells revealed: megalocytes, 473; microcytes, 328; poikilocytes, 45; megaloblasts, 23; normoblasts, 19; leucocytes, polymorphonuclear, neutrophile, 68.6 per cent.; eosinophile, 2.26 per cent.; large lymphocytes, 2.52 per cent.; small lymphocytes, 26.46 per cent.; myelocytes (neutrophile), 63 per cent. Proportion of white to red cells, 1 to 113. Most of the erythrocytes were about the average in size

At this time a clinical diagnosis was proposed of multiple periosteal sarcoma, with attending severe secondary, probably pernicious, anemia.

Report of Autopsy.—Nov. 20, 1902. General emaciation very marked, the skin being extremely pale. No change noticeable in the cervical, axillary, clavicular, and inguinal lymph nodes.

Skull and Cranial Contents.—After removing the scalp seven distinct circumscribed tumors are observed attached to the skull, appearing as cushion-like growths and distributed as follows: One over the frontal bone, two on the left parietal, one on the right parietal, one over the right mastoid, and two on the occipital bone. The tumors are of soft consistency and vary in color from deep gray to pinkish and reddish gray; in diameter they range from 3.5 to 6 centimeters. The growths extend above the bone about one centimeter, and are well defined from the skin and subcutaneous tissues. After the skull cap is removed the tumors are seen to have completely penetrated both the outer and inner tables, the latter presenting a distinct honeycomb appearance; the growths also involving the dura mater.

A considerable amount of subdural serous effusion is present. The brain is pale and anemic, but otherwise negative.

Diaphragm at Fourth Rib, Right and Left.—Pleura and pericardium negative; heart valves intact, musculature anemic and somewhat atrophic. The lungs are pale and freely movable with some passive congestion in the lower lobes; bronchi pale, containing a grayish foamy liquid. Esophagus contains a small amount of foamy mucus, mucosa pale.

No fluid in the peritoneal cavity. The spleen is not enlarged, on section it is a pale brownish red; pulp is soft and bleeds readily. The liver appears slightly enlarged; the surface is smooth; on section the surface is cloudy, and of a pale red chocolate color; a slight fatty smear is left on the knife; outlines of lobules distinct; throughout the liver substance a limited number of light-colored circumscribed areas are noted, ranging from 0.3 to 0.8 centimeters in diameter and having the macroscopic appearance of the cut surface of the cranial tumors. Gall bladder negative. Kidneys are pale; a retention of fetal lobulation exists, otherwise negative. Bladder negative. Pancreas and suprarenals negative. The stomach and intestinal mucosa is pale, but negative in other respects. Mesenteric glands are negative.

In the retroperitoneal region a marked enlargement is noted in the prevertebral lymph nodes or hemolymph glands; extending from the brim of the pelvis upward along the aorta and vena cava are sixteen enlarged and dark red glands, forming in reality a dense mass involving an area of 5x12½ centimeters; the larger glands being 2x3½ cm. in dimensions, and of a dark red color; the smallest examples having a coffee-bean shape, 0.6x1 cm. in diameters; pale and red nodes are noticed placed side by side. A few of the smaller glands extend along the renal vessels. The entire mass is imbedded in fat and very closely connected with the surrounding blood vessels.

The long bones were not opened owing to the restrictions placed on the autopsy, but the cross section of the sternum presented the hemorrhagic appearance of marrow peculiar to severe anemias. The extreme emaciation of the body permitted a good examination of the surface of the different bones, and disclosed an absence of any periosteal growths or enlargement of the bones.

Histologic Examination.—The tissues were all studied in serial paraffin section, and stained by hematoxylin and eosin, Van Gieson's, and Mallory's stain for connective tissue, and the potassium ferrocyanid method for demonstrating hemosiderin.

Periosteal Tumors.—While the general histologic picture is that of round cell sarcoma, there is some degree of variation between the several tumors. The cell element consists of a round cytoplasmic mass with a nucleus rich in chromatin, the latter varying in size, frequently granular, and seen in varying stages of mitosis; a delicate intercellular reticulum is present; the fibrous tissue stroma following principally the blood channels forms an alveolar arrangement in some portions and presents the type of an alveolar sarcoma; again the prominence of blood vessels and hemorrhage give a picture resembling angiosarcoma, while the light gray colored tumors in section reveal a type like lymphosarcoma.

The ordinary lymph nodes present no definite histologic changes. Heart and lungs are negative. Brain is negative.

Spleen reveals a slight degree of fibroid hyperplasia; hemasiderosis is very marked. Adrenals, kidneys and pancreas are negative. The stomach and intestines reveal some signs of catarrhal inflammations.

Liver.—Cloudy swelling in the cells, lobules are not well defined, and interlobular interstitial connective tissue is not increased. Distributed throughout the liver substance are well-circumscribed areas representative of metastatic growths secondary to the periosteal tumors, evident by reason of their identity in structure. Their histology consists of small round cells arranged in distinct alveoli formed by rather delicate fibers of connective tissue, resembling the picture of alveolar sarcoma. Hemasiderosis is present.

Hemolymph Nodes.—The smaller nodes 0.5 cm. in diameter present a histologic picture resembling the so-called marrow-lymph variety of hemolymph nodes, consisting of well-defined sinuses apparently lined by endothelium; throughout these sinuses a delicate reticulum is noted holding in its meshes principally red blood cells and a few leucocytes. Among the red cells normoblasts are observed and an occasional megaloblast. A few eosinophiles are seen. Some of the blood sinuses are very short and irregular. The constituent lymphoid tissue adjacent to the blood sinuses is made up of columns or bands of cells chiefly lymphoid (small mononuclear) in character; these cells also lie in a very delicate reticulum; large mononuclear lymphocytes are observed in small numbers, frequently mitotic figures are seen and again some of the nuclei appear also completely disintegrated. Large collections of hematic pigment are seen in the lymphoid area and the iron reaction is brought out by application of the potassium ferrocyanid stain. A few hyaline bodies are noted.

In the larger examples of hemolymph nodes, especially those having dimensions 2x3½ centimeters, the round or lymphoid cell infiltration completely obscures the essential hemolymph structure.

The cells are arranged in columnar-like collections divided by bands of fibrous connective tissue of greater or less density, forming alveolar areas resembling the picture of alveolar sarcoma; again in some areas the resemblance to lymphosarcoma is very striking. The cells contain large round granular nuclei, with varying figures of mitosis, resembling the cells of round-cell sarcoma.

In the peripheral portions of the enlarged nodes well-defined areas of red blood cells are seen and the lumina of well-formed blood channels are observed, some of which resemble closely the sinuses of hemolymph nodes except that the delicate intercellular reticulum is not apparent. Small areas of caseation are present in some of the cell areas. In all of the enlarged hemolymph nodes hematic pigment is abundant, some of which responds to the iron reaction, phagocytes containing hematic pigment being noted in the blood channels.

Unfortunately the circumstances of the autopsy prevented the histologic examination of the bone marrow.

Summary.—The features that invite interest in connection with this case are the multiple periosteal sarcomata confined to the cranial periosteum, the secondary involvement of hemolymph nodes, and the attending severe, probably pernicious, anemia. The origin of the tumors from the periosteum seems evident by reason of the intimate connection with the surface of the bones; the involvement of the inner table and extradural tissue being the result of extension.

If one of the periosteal tumors is to be regarded as the primary growth and the others as secondary nodules, it would seem like rather an unusual form of metastasis, and I prefer to regard them all as primary tumors.

It must be evident to all that considerable confusion exists in the literature on the various sarcoma-like tumors involving the osseous system, especially those which are attended by leukemic or pseudoleukemic change in other tissues. This is principally true of the multiple periosteal tumors having the histologic character of round cell sarcoma and described as chloroma and lymphosarcoma in which the relationships to pseudoleukemia is rather intimate.

Chloroma is frequently characterized by multiple periosteal plate-like growths especially of the cranium with metastasis in the lymph nodes, different portions of the skeleton and internal organs. In structure they resemble lymphoma or lymphosarcoma and contain a greenish pigment.

The absence of pigment in the case in question, especially in the fresh specimens, excludes chloroma, but in some other respects there is a great resemblance to this peculiar tumor process.

Closely related to chloroma are those non-pigmented pseudoleukemic periosteal tumors having the structure of lymphosarcoma which have been extensively considered by Claus under Marchand's direction, the same appearing as cushion-like growths on the skull, sternum, ribs, pelvis, spinal column and femur with tumor formations in the tonsils, lymph, nodes, liver, and marked enlargement of the spleen. Lazarus, Gussenbauer, Chiari, and Dittrich have described more complicated cases in which the spread of tumors in internal organs was more prominent, giving the impression of a general metastasis, the relation to the primary periosteal localization of the malignant lymphoma, though, being well defined.

As to the tumor nodules in the liver and involvement of the hemolymph nodes with their identity in histologic structure to the primary cranial growths, the findings warrant regarding them as secondary or metastatic formations.

The close resemblance of the arrangement of cells, with numerous mitotic figures in the enlarged hemolymph nodes to that in the periosteal growths is so striking as to permit of no other conclusion than that they are metastatic.

Both of the secondary manifestations must be regarded as examples of vascular metastases, and it must be due to the connection of the hemolymph nodes with the circulatory system that they are more liable to involvement than the other lymphoid structures throughout the body. The fact that the lungs were not involved bv metastasis may be attributed to the relatively small size of the constituent tumor cells permitting them to pass through the pulmonary circulation.

That the attending severe, probably pernicious, anemia is the result of hemolysis, is evident from the general blood changes and the hemosiderosis in the spleen, liver and hemolymph nodes. The blood findings are very similar to those of pernicious anemia.

This case offers a further illustration of the relationship between changes in hemolymph nodes and the severe anemias. According to Warthin there is a certain amount of normal hemolysis taking place in these glands, and the hemolysis of severe or pernicious anemia differs from the normal only in degree. As the last named condition is probably due to some circulating poison, the nature of which is as yet unknown, so in the case described it is a circulating sarcoma process, which by reason of its involvement of the hemolymph nodes led to an increased hemolysis in these structures.

It is in this class of sarcoma-like tumors, including chloroma, and those of lymphosarcoma and pseudoleukemic type that a parasitic cause will probably ultimately be discovered.

DISCUSSION.

Dr. E. R. LeCount, Chicago—There is an intimate connection between the tumors in the case described by Dr. Bierring with the growths observed on the one hand, as multiple myelomas, and on the other in cases of chloroma. Had the tumors described in this case been possessed of a greenish cast Dr. Bierring would no doubt have considered his case as one of chloroma. The absence of the peculiar color does not seem to me sufficient reason for excluding the growths in this case from those in pseudo-leukemia, chloroma, multiple myeloma and acute leukemia. Therefore, I would object to the term sarcoma and prefer some name which would indicate their position correctly as examples of multiple growths unconnected with sarcoma in method of origin, growth and extension; for example, "multiple periosteal lymphomata" or "a case of chloroma with absence of the usual pigmentation." The term sarcoma has little to do with tumors that are primarily multiple.

Dr. Henry A. Christian, Boston—Dr. Bierring speaks of the difficulty in such tumors of determining which is the primary growth. The relation that exists between the more or less diffuse processes in bones and definite tumor masses is a very close one, and to say that a certain growth is primary and the others are metastases is very difficult in a case like this.

A great many similar examples have been reported and I would like to add one. It was a case in which both kidneys were very much enlarged, four or five times their normal size, but they were not distorted and there were no definite tumor masses in the kidneys. They were both of the same size. Microscopic study showed the kidney tubules to be separated by a growth which proved to be of the nature of a round cell sarcoma, a diffuse sarcoma appearing simultaneously in both kidneys. The bone marrow of the femur showed similar changes. The question is, whether we have here a tumor of the bone marrow metastasing in the kidneys, the development in the kidneys of a tumor, bilateral and simultaneous in origin, or have we some general diffuse condition of the bone marrow which has not found its expression in cellular changes in the blood vessels as in leukemia, but has affected certain organs in a similar manner as the bone marrow.

Dr. Walter L. Bierring, Iowa City, Iowa—I appreciate what Dr. LeCount has said in regard to the terminology of this condition, but I labored for a long time in trying to name this process, and while I know that the term sarcoma is not entirely satisfactory, it seems to me that the various round-cell growths variously termed as chloroma, lymphosarcoma and small round-cell sarcoma are all more or less connected, and I think some day they will be cleared up and shown to be of parasitic origin.

I made a number of inoculations from fresh tissue material under proper precautions on the various culture media, but was unable to obtain any results. All tests for albumin and albumose in the urine were negative.

I regret that the restrictions of the autopsy prevented an examination of the long bones, but in this case I am still inclined to think that they were not particularly affected.

THE APPARENT IMMUNIZING VALUE OF ATTENUATED TUBERCLE BACILLI.

E. A. DE SCHWEINITZ, M.D.
Director of Biochemic Laboratory, Bureau of Animal Industry,
Department of Agriculture, and Dean, the
Columbian Medical School.
WASHINGTON, D. C.

The recent attention which has been drawn to the difference in virulence of tubercle bacilli from various animals, and the publication by Behring of the production of immunity to tuberculosis in cattle by the use of tubercle bacilli of low virulence, have suggested that if perhaps a little more attention had been given to some work published in December, 1894, there would have been less tendency in some quarters, at any rate, to assume an absolute difference between tubercle bacilli obtained from men and those obtained from cattle. The published works of the writer and Dorset and Schroeder, Ravenel, Nocard and that of others, have shown so conclusively that it is possible to obtain tubercle bacilli, sometimes from the sputum of adults and frequently from intestinal lesions in children, which will produce tuberculosis in cattle when the latter are inoculated subcutaneously, that it seems now almost a waste of time to discuss a question which has been so positively proved. Considering further the numerous cases of accidental infection with bovine tuberculous material, and also that monkeys are more readily infected with bovine tuberculosis than with human tuberculosis, and it is well known that monkeys are more closely allied to man than any other animal, the possibility of the intercommunicability of bovine and human tuberculosis has been well established. The fact, further, that tubercle bacilli as well as other bacilli become more or less attenuated, depending on their growth on artificial media outside of the animal body or on their cultivation within the animal body, or in other words, the fact that they are easily influenced like other plants, by changes in soil and climate, has also been well proven by ourselves and others.

Our work, published in 1894,[1] was the first to show that guinea-pigs that had received large doses of attenuated human tubercle bacilli, those bacilli that had largely lost their virulence or power of producing disease, were rendered resistant and immune to subsequent inoculation with tuberculous material of bovine origin. Further, in 1894-5-6-7-8, cattle and various other large and small animals were injected with frequent doses of attenuated tubercle bacilli and in some cases subsequently tested by inoculation with bovine tuberculous material. While the earlier works on the effect of large doses and the apparent immunizing value of attenuated human cultures on cattle were reported in 1896, Bulletin No. 13, Bureau of Animal Industry, and in the Proceedings of the Association of American Physicians, 1897, the results of the practical tests on some of these animals with tuberculous material have never been recorded, but may be of interest now. The practical treatment of these animals was made for me at the Experiment Station of the Bureau of Animal Industry by Dr. E. C. Schroeder.

In one of our earlier experiments begun in 1894, an old cow, 285, from a tuberculous herd, which on physical examination appeared to be clearly tuberculous, was given large injections of tuberculin, subcutaneously. The first dose used was 25 c.c. and the amounts were gradually increased so that between August, 1895, and

---

[1] Medical News.

October, 1897, when the animal was killed, it had received altogether 19,500 c.c. of tuberculin, as much as 1,500 c.c. being given at one dose. After four months' treatment with tuberculin the cow seemed to improve considerably. This apparent improvement, however, did not persist and the autopsy, when made in 1897, showed a most generalized tuberculosis, all stages of the disease being apparent. If the treatment with tuberculin had any beneficial effects the disease was so far advanced when the treatment was begun that no practical benefit could be secured.

IMMUNITY TESTS ON CATTLE.

On July 26, 1894, cow 217 received an injection in the jugular vein of 16 c.c. of a suspension of an attenuated human tubercle culture then in the 17th generation. This injection produced a large swelling at the seat of inoculation, but no other evidence of tuberculosis was noted.

On Nov. 28, 1894, this same animal received an abdominal injection of 6 c.c. of the 23d generation of attenuated culture. On Jan. 25, 1895, it received an intrathoracic injection of 6 c.c. of unfiltered culture of the 26th generation. On March 5, 1895, it received an injection into the right side of the chest of 16 c.c. of the 33d generation of a tubercle culture. Between April, 1895, and July, 1897, the animal received subcutaneous injections of attenuated tubercle culture, as much as 2,000 c.c. being given at a single injection. Altogether, therefore, it had received one intravenous, two intrathoracic, two abdominal and thirty-nine subcutaneous injections of attenuated tubercle culture. As the animal appeared to be in good health and well on Feb. 22, 1898, it received an injection into the thoracic cavity of 10 c.c. of a turbid triturate of a tuberculous gland obtained from a cow. This gland contained many virulent bacilli, as proved by inoculation tests. On Sept. 20, 1898, this cow was killed, and postmortem examination showed it to be free from disease, indicating, therefore, that neither the attenuated human culture nor the bovine material had produced tuberculosis.

Another cow, 297, the offspring of the tuberculin cow just referred to, 285, was tested with tuberculin on Nov. 19 and 20, 1894, and found free from disease. On Nov. 24, 1894, it received an injection in the abdominal cavity of 6 c.c. of the 23d generation of a tubercle culture. The temperature as taken for ten days following the injection seemed to indicate no disease. Between Jan. 25, 1895, and July 25, 1895, it received five subcutaneous injections of attenuated tubercle culture, about 250 c.c. being given altogether. In August, 1895, it received an injection of a bovine culture. Beginning again Dec. 2, 1895, it received large subcutaneous injections of attenuated tubercle culture, about 13,500 c.c. of the material being given altogether. On Feb. 22, 1898, at the same time that 217 was inoculated, it received an intrathoracic injection of some of the same tuberculous material as that given to 217. Killed on Sept. 20, 1898, when apparently in good condition, the autopsy showed a few tubercular nodules in the udder, while the superficial lymph glands, liver, kidneys and spleen were normal. There were, however, some large tubercular masses on the pleura. The tubercular lesions appeared to have come from the first inoculation with bovine material.

In April, 1896, two calves were inoculated with smaller doses of attenuated tubercle culture, subcutaneously, two animals with serum from cow 285, which in its turn, as reported, had received large doses of tuberculin, and two animals were reserved as checks. These calves subsequently tested with bovine tuberculous material did not show the same amount of resistance as did those first inoculated. One of the calves which had received preventive inoculations of the serum from cow 285 seemed to possess immunity. So far as the records of the check inoculated with bovine material show (these latter records are unfortunately incomplete) the check contracted tuberculosis from which it died in September, 1896, while the preventively inoculated animals had shown considerable resistance. The established immunity was not as good as that obtained in the first experiments. In the first tests several intravenous inoculations, as well as subcutaneous, were made. In the second set only a small number of subcutaneous inoculations were made.

These experiments on cattle considered in connection with those on guinea-pigs showed that as it was possible to vaccinate against bovine tuberculosis by means of tubercle bacilli of human origin, then we are simply dealing with tubercle bacilli of varying degrees of virulence, and not tubercle bacilli that are really different from each other. The readiness, as we have shown, with which not only human but, as may be seen from the records attached, also bovine tubercle bacilli may be attenuated, and the ease with which, according to Nocard, avian tubercle bacilli may be converted into those of a mammalian character, all go to prove the intimate relationship of bacilli obtained from various sources.

Steer 242 was drenched with bovine tuberculous material on Jan. 10, 11, 13 and 21, 1902. On February 17, 18 and 26 of the same year, tested with tuberculin, a positive reaction was given. On October 6, about nine months after the first drenching, this animal was killed. A few small foci of a tuberculous character were found in the mediastinal and in the lymph glands at the entrance of the thorax; otherwise no evidence of tuberculosis.

On Nov. 2, 1901, bull 223 was inoculated subcutaneously with 10 c.c. of bovine culture No. 3 (Smith). On Jan. 21, 1902, and April 18, 1902, reactions after tuberculin injections were noted. On Oct. 2, 1902, when the animal was killed, its general condition was excellent. At the seat of inoculation there was a patch of induration about six inches in diameter in which were imbedded small abscesses containing a soft, cheesy material. The shoulder glands on the side of infection, both deep and superficial, were enlarged and sprinkled with necrotic foci. The mediastinal glands contained numerous necrotic foci. No other lesions of any kind were present.

This animal showed very much less tuberculosis than that found after six weeks in a calf which received, subcutaneously, injections of material from tuberculous cultures isolated from children. Compared with the record of another heifer, 284, which had been inoculated with a different virulent bovine culture (a culture that had been isolated from a spontaneous case of disease occurring at the Experiment Station), and which showed after eight weeks very generalized tuberculosis, it is very evident that the bovine germ by cultivation loses in violence and in ability to produce disease just as well as the human bacillus. It becomes attenuated. This is another strong point and emphasizes the influences of environment on the virulence of bovine as well as human bacilli.

Our earlier work and results in this connection have therefore simply been confirmed by the recent experiments of MacFadyean, Behring, Pearson and Gilliland and others.

DISCUSSION.

Dr. L. Hektoen, Chicago—Did I understand the author to mean by attenuated bacilli those that have been cultivated artificially for some considerable time?

Dr. M. Dorset, Washington, D. C.—This culture referred to is one which lost its virulence after having been cultivated for several years and one which will not kill guinea-pigs even in large doses.

Dr. Joseph McFarland, Philadelphia—Is that a peculiarity of this bacillus or is the same true of all bacilli? Do they all become attenuated?

Dr. M. Dorset, Washington, D. C.—This particular human culture is the most attenuated form we have. We have some human tubercle bacilli that have been growing for ten years without passage through an animal, and they are still quite virulent for guinea-pigs. This particular culture does seem to be an exception.

Dr. Victor C. Vaughan, Ann Arbor, Mich.—I would like to ask the gentlemen present if it has been their experience that tubercle bacilli become attenuated after having been grown for many generations?

Dr. Joseph McFarland, Philadelphia—I brought back with me from Berlin in 1895 a tubercle bacillus that had been isolated by Koch many years ago, and I kept it growing for more than five years. At the end of that time it seemed to have retained its virulence. I never went through any quantitative method of determining this, but relatively its virulence did not seem to be diminished. Unfortunately I lost the germ and could not continue the experiment.

Dr. Victor C. Vaughan, Ann Arbor, Mich.—In 1888, when I was a student in Koch's laboratory, Professor Fraenkel gave me a culture of the tubercle bacillus which he said was the 112th generation of one of the first cultures made by Professor Koch in 1882. I used that germ and its descendants in experiments on guinea-pigs and rabbits and it retained its virulence until about 1896. During the interval between 1888 and 1896 no year passed in which I did not inoculate animals with this germ, and in every case it was found to be virulent. In 1896 it began to lose its virulency for guinea-pigs, and soon ceased to have any effect even in large doses. Two years ago I sent to Dr. Lartigau a culture of this germ and a few weeks ago I had a letter from Dr. Baldwin of Saranac, saying that he had obtained the culture from Dr. Prudden and had experimented with it and that his experiments had confirmed my statements. The germ has completely lost its virulence so far as guinea-pigs were concerned.

EXPERIMENTS WITH RENNET AND ANTI-RENENE.

JOSEPH McFARLAND, M.D.
PHILADELPHIA.

In 1899 Morgenroth published a paper entitled "The Antibody of Rennet," containing a description of certain work that he had done in support of Ehrlich's chemical theory of the toxin-antitoxin reaction. So far as I know, Morgenroth's work met with universal acceptance without having been subjected to experimental confirmation, nor did I think it worth while to confirm it or make any addition to what Morgenroth had found until the specific precipitates began to attract attention, when their study led me to experiment with antipeptone, antivenene and antirenene.

The antirenene was prepared solely for the purpose of securing the precipitate, but as I found it possessed the power of inhibiting the coagulant action of rennet on milk, I continued to investigate the subject until I found in it a confirmation of what Morgenroth had done, and found myself able to make a few additional contributions to the subject.

Morgenroth's experiments were performed on goats, which were injected with rennet prepared by Witte in Rostock, the activity of this rennet being 1-3,000,000. The sterility of the rennet solution was secured by the addition of iodin (1 c.c. of a 1-10 iodin solution to each 10 c.c. of the rennet solution permitted to stand 1 hour at room temperature), and no abscesses followed its employment.

The goat was given increasing doses of the rennet solution administered by subcutaneous injection until 6.5 grams at a dose were administered. After each injection the temperature rose to about 41.4 C., without any disturbance of the general condition or appetite, and without any observable diminution of the body weight. Of the two goats thus treated, one produced a considerable quantity of the antibody, the other attained an extremely small degree of immunity, although both were subjected to exactly the same treatment.

The observation of Schepilewski, that an injection of sterile rennet produced amyloid disease, was not confirmed, as both of the goats remained healthy for more than a year after the close of the experiment.

Morgenroth's studies of the antirenene were made with the blood serum and milk of the goats. The standard rennet solution for testing the antibody consisted of a watery extract of the rennet powder in a 10 per cent. sodium chlorid solution, to which was subsequently added an equal quantity of glycerin and 10 per cent. sodium salt solution. It was found that such a solution contained 2 per cent. of the rennet powder, and could be kept for more than a year and a half unaltered. The presence of the antibody in the serum was tested on cow's milk saturated with chloroform by a long continued shaking in a shaking apparatus and then preserved in the cold.

The method for testing adopted by Morgenroth was as follows: His rennet had the power of coagulating milk in a proportion of 1 part in 3,000,000, but when the milk received an addition of 2 c.c. of the serum of an immunized goat, a proportion of rennet equal to 1-30,000 failed to produce coagulation, though a proportion of 1-25,000 produced a firm clot, so that the serum had the power to neutralize 100 times the coagulating rennet dose, and to thicken the milk 200 times the usual dose was required.

The serum from the other goat that did not attain a high degree of antirenene was so much less active that 2 c.c. inhibited in a proportion of 1-120,000 only. The antibody was extremely unstable, and when preserved with chloroform and kept in an ice chest, its activity disappeared in a few months.

My own experiments were conducted on a different plan and with different animals. Rabbits were chosen for the experiment, and at weekly intervals were given intraperitoneal injections of considerable quantities of the standard rennet solution. The rennet employed is a granular, dry powder of a yellow-cream color, freely soluble in water and physiologic salt solution. My standard solution consisted of a 5 per cent. solution in physiologic salt solution, saturated with chloretone. This preparation was found to be so stable that its strength did not alter on keeping for several months, and it was so active that 1/2,500 of a c.c. produced a firm coagulum in standardized milk in between one and two hours. The strength was, therefore, equivalent to 1-500,000. Each injection of 5 c.c. given to the rabbit contained 0.25 of a gram of the pure rennet.

The rabbits on which my experiments were made weighed in the neighborhood of 1.5 kilograms each. Morgenroth does not give the weight of his goats, and I am not sufficiently familiar with goats to know exactly what they weigh, but presume an average goat would weigh about 50 kilograms. This being the case, the goats weighed approximately thirty times as much as the rabbits, and basing the calculation on body weight would presumably endure about thirty times as much rennet. My experiments were conducted without any knowledge as to the quantity of rennet administered by Morgenroth to his goats. On subsequently looking it up I found that the largest quantity they received was 6.5 grams. Since the rabbits received 0.25

of a gram at a dose, the goats on the same ratio should have received about 8 grams. This would suggest that the rabbits should have attained a higher degree of immunity and produced a stronger antibody than the goats, supposing their ability to produce the antibody about equal. We find, however, that the rennet with which Morgenroth performed his experiments had a strength of 1-3,000,000, or six times that of my rennet. It is thus evident that in proportion to their weight, my rabbits did not receive nearly as much rennet as Morgenroth's goats, and it is not surprising that I found the anticoagulant powers of their serum considerably less. This is, however, by no means a necessary inference, as Morgenroth showed that of his goats, one produced a serum whose anticoagulant power was 1-25,000, while the other was only 1-120,000, thus confirming what is a familiar observation to every one who has experimented with antibodies, viz., that different animals treated in the same way attain very different degrees of immunity, and very different kinds of antibodies in the blood.

Three rabbits were employed for the experiment. The first died after a single injection. At the necropsy I found an extensive serofibrinous inflammation of the pericardium, pleura and peritoneum, and with more or less pneumonia. The exudates contained several different bacteria. The second animal endured about five injections and then died with identical lesions. In the exudates and blood several different bacteria were found. Both the animals seemed to die early in the night, and when bacterioscopic examination showed that several bacteria were present in the exudates, it was not thought worth while to endeavor to isolate the one responsible for the infection. It is interesting to notice, however, that fibrinous exudates occurred in both these animals.

The third rabbit survived a number of injections of 0.25 of a gram of the rennet and was finally bled to death, the serum being carefully separated for study, and extracts of the different organs of the body made in order to determine whether either rennet or antirenene might be contained in the tissues. For this purpose extracts were made of the medulla oblongata, kidney, liver, pancreas, adrenal, bone marrow, lung, voluntary muscle, stomach, large intestine and small intestine. These extracts were prepared by adding to each fragment of tissue ten times its weight of physiologic salt solution (a gram was considered equivalent to 1 c.c. of salt solution). The organs were finely crushed in a mortar, being reduced to a pulp before the salt solution was added. The mixture was then placed in a test tube and kept in the cold over night. The rabbit, therefore, furnished blood serum, organic extracts and urine for further study.

In order that the investigations might be accurate, it was necessary to standardize the milk, and for this purpose chloroform and formaldehyd were first tried. The chloroform was found to be less reliable than was hoped, and the formaldehyd was found to diminish the coagulability of the milk. I, therefore, tried chloretone and found that by saturating the milk with this I was perfectly able to protect it against subsequent micro-organismal contaminations, without in any way inhibiting its coagulating power.

As the layer of cream which soon rises and covers the surface of milk kept at the temperature of the body interferes with determining whether the milk has thickened from the presence of the rennet, I found it expedient to use "separator milk" from which the cream was removed. The reaction of the milk affects the action of the rennet; acid milk coagulated much more completely than neutral or alkaline milk. By securing milk fresh from the dairy and immediately saturating it with chloretone, I was able to secure a sufficiently accurate standard, as there was very little variation in the reaction of fresh separator milks, and the saturation with chloretone prevented the development of acidity by bacterial action. The reaction of the milks employed was acid, the acidity varying from 16 to 18 c.c. of normal caustic soda solution being required to neutralize one liter. The difference was so slight that though we tested it carefully it did not in any way seem to modify the action of the rennet, and it is thought not worth while to correct it.

It is well known that the temperature affects the action of rennet, which is much more energetic at high than at low temperatures. Morgenroth preferred to afford his rennet twenty-four hours in which to effect coagulation, keeping the milk in the meantime on ice. Inasmuch as we had eliminated the possibility of any bacterial change in the milk, we were able to keep it at the temperature of incubation, and found that 0.000002 of a gram of rennet added to 10 c.c. of milk invariably produced a firm clot in between one and two hours. We, therefore, adopted the temperature of 37 C. as a standard for the experiments.

In studying the action of the antibody we, therefore, had the following standard conditions:

1. A solution of rennet of which 0.000002 of a gram invariably coagulated 10 c.c. of milk kept at 37 C. in between one and two hours.
2. Milk of a reaction necessary for the appropriate action of the rennet and perfectly preserved from bacterial contamination or alteration either from the production of enzymes or the formation of acids, by saturation with chloretone. (Of this milk, 10 c.c. were used for each test).

The first series was an endeavor to determine whether the rennet injected into the animal was stored up in any of its tissues, and for this purpose 2 c.c. of each of the tissue extracts prepared was added to 10 c.c. of milk and incubated the appropriate length of time. This experiment we made as soon as the extract was prepared.

TABLE 1.—THE FOLLOWING MIXTURES WERE PERMITTED TO STAND FOR 12 HOURS:

10 c.c. Milk + 1 c.c. Extract of Kidney (freshly prepared)	=0
“ “ + “ “ “ Liver	=0
“ “ + “ “ “ Pancreas	=0
“ “ + “ “ “ Adrenal	=0
“ “ + “ “ “ Bone marrow	=0
“ “ + “ “ “ Lung	=0
“ “ + “ “ “ Voluntary muscle	=0
“ “ + “ “ “ Brain	=0
“ “ + “ “ “ Blood serum	=0
“ “ + “ “ “ Urine	=0
“ “ + “ “ “ Large intestine	=0
“ “ + “ “ “ Small intestine	=+
“ “ + “ “ “ Stomach	=+

The coagulation produced by the extracts of stomach and small intestine probably depends on the presence of rennet naturally formed in the stomach. No rennet existed in any of the other extracts, in the blood serum or in the urine. A similar series was made after permitting the sodium chlorid solution to act on the crushed organs for about 20 hours.

TABLE 2.

10 c.c. Milk + 1 c.c. Extract of Kidney*	=0
“ “ + “ “ “ Liver	=0
“ “ + “ “ “ Pancreas	=0
“ “ + “ “ “ Adrenal	=0
“ “ + “ “ “ Bone marrow	=0
“ “ + “ “ “ Lung	=0
“ “ + “ “ “ Voluntary muscle	=0
“ “ + “ “ “ Brain	=0
“ “ + “ “ “ Blood serum	=0
“ “ + “ “ “ Urine	=0
“ “ + “ “ “ Large intestine	=0
“ “ + “ “ “ Small intestine	=0
“ “ + “ “ “ Stomach	=0

* After 24 hours' maceration.

The next experiments were made for the purpose of determining whether any of the organic extracts contained important quantities of antirenene, and were made with extracts which had been allowed to stand in the cold for about twenty hours.

TABLE 3.—THE FOLLOWING WERE PERMITTED TO STAND FOR 3 HOURS:

10 c.c. Milk + 1 c.c. 20-hour Extract of:

Kidney + rennet 0.000002 gr	=+
Liver + rennet 0.000002 gr	=+
Pancreas + rennet 0.000002 gr	=+
Adrenal + rennet 0.000002 gr	=+
Bone marrow + 0.000002 gr	=+
Lung + rennet 0.000002 gr	=+
Voluntary muscle + rennet 0.000002 gr	=+
Brain + rennet 0.000002 gr	=+
Large intestine + rennet 0.000002 gr	=+
Small intestine + rennet 0.000002 gr	=+
Stomach + rennet 0.000002 gr	=+

Although these experiments were crudely made, they seemed to indicate the absence of important quantities of antirenene in the tissues of the rabbit's body. It might be well to remark that the softest coagulum in the series was that in the tube to which the bone marrow had been added.

The next experiments were made to determine the ability of the blood serum to inhibit the action of the rennet. I find that my method of experimentation differs markedly from that of Morgenroth. Morgenroth used a measured quantity of milk containing an equal proportion of serum and added varying quantities of the rennet. I preferred to experiment by a method more nearly resembling that by which the antitoxic unit is determined in the estimation of the value of antidiphtheritic and antitetanic serums. I, therefore, employed 10 c.c. of milk to which was added exactly the quantity of rennet known to effect its coagulation, and then varying quantities of serum, until I determined the least quantity that would inhibit coagulation.

Table 4.—Duration of the Experiment 3 Hours.
Temperature 37 C.

10 c.c.	Milk	+	0.00002	gr.	rennet	+	serum	1 c.c..........	=0
"	"	+	"	"	"	+	"	0.7 c.c.........	=0
"	"	+	"	"	"	+	"	0.6 c.c.........	=0
"	"	+	"	"	"	+	"	0.5 c.c.........	=0
"	"	+	"	"	"	+	"	0.4 c.c.........	=0*
"	"	+	"	"	"	+	"	0.3 c.c.........	=0†
"	"	+	"	"	"	+	"	0.2 c.c.........	=+
"	"	+	"	"	"	+	"	0.1 c.c.........	=+
"	"	+	"	"	"	+	"	0.09 c.c.......	=+
"	"	+	"	"	"	+	"	0.08 c.c.......	=+
"	"	+	"	"	"	+	"	0.07 c.c.......	=+
"	"	+	"	"	"	+	"	0.06 c.c.......	=+
"	"	+	"	"	"	+	"	0.05 c.c.......	=+
"	"	+	"	"	"	+	"	0.04 c.c.......	=+
"	"	+	"	"	"	+	"	0.03 c.c.......	=+
"	"	+	"	"	"	+	"	0.02 c.c.......	=+
"	"	+	"	"	"	+	"	0.01 c.c.......	=+
"	"	+	"	"	"	+	"	0.001 c.c......	=+
"	"	+	"	"	"	+	"	0.0005 c.c.....	=+
Control 10 c.c.	milk	+	0.00002	gr.	rennet	+	serum..........		=0

* Soft clot. † Very soft clot.

In this way I showed that the serum effected a distinct inhibition of coagulation, causing the rennet to become inactive in tubes containing 0.5 c.c., or more, of the serum.

The next series of experiments had to do with the specific precipitate, which I expected to find much more delicate, as a means of determining the presence of the antibody rather than the interference with coagulation. Dilutions of the serum and rennet in which the proportions were known, were prepared, placed in small test tubes and kept at the standard temperature. The result was not delicate, as I had anticipated, as is shown by the following table. The quantities of rennet and serum were each diluted with several cubic centimeters of physiologic salt solution, poured together, well shaken, placed in a narrow test tube, and incubated for twenty-four hours:

TABLE 5.

0.00002	gr.	rennet	+ 0.4 c.c. serum	=+
"	"	"	+ 0.3 c.c. serum	=+
"	"	"	+ 0.2 c.c. serum	=+
"	"	"	+ 0.1 c.c. serum	=+(?)
"	"	"	+ 0.01 c.c. serum	=0
"	"	"	+ 0.005 c.c. serum	=0
"	"	"	+ 0.0033 c.c. serum	=0
"	"	"	+ 0.0025 c.c. serum	=0
"	"	"	+ 0.002 c.c. serum	=0
"	"	"	+ 0.001666 c.c. serum	=0
"	"	"	+ 0.00142 c.c. serum	=0
"	"	"	+ 0.00125 c.c. serum	=0
"	"	"	+ 0.0011 c.c. serum	=0
"	"	"	+ 0.001 c.c. serum	=0

The large quantity of serum required to inhibit the action of the rennet perplexed me, as it seemed not to be in keeping with what was known about other antibodies. It, therefore, occurred to me that the action of the rennet on the milk might take place too rapidly to afford anything but an overwhelming quantity of the serum an opportunity to inhibit it, and that if I would make mixtures of rennet and the antibody in varying proportions and permit them to stand at the temperature adopted for the standard for a number of hours, the rennet might be destroyed by the antibody in very much smaller quantities than was necessary when both were immediately added to the milk. I, therefore, prepared a number of such mixtures and a correspondingly great dilution of rennet, permitted them to stand over night in the incubator and then added the appropriate quantities to the milk. The result showed that under these conditions the action of the antibody on the rennet was very energetic and entirely confirmed by expectations. Instead of requiring 0.5 c.c. to inhibit coagulation, I now found 0.0005 c.c. to be sufficient, this being the least quantity investigated.

TABLE 6.—TIME, 3 HOURS. TEMPERATURE, 37 C. CONTROL. 10 C.C. MILK + (0.00002 GR. RENNET INCUBATED 24 HOURS) =+.

10 c.c. milk	+	(0.00002 gr. rennet	+ 0.4 c.c. serum)	=0
" "	+	" " "	+ 0.3 c.c. serum)	=0
" "	+	" " "	+ 0.2 c.c. serum)	=0
" "	+	" " "	+ 0.1 c.c. serum)	=0
" "	+	" " "	+ 0.01 c.c. serum)	=0
" "	+	" " "	+ 0.005 c.c. serum)	=0
" "	+	" " "	+ 0.0033 c.c. serum)	=0
" "	+	" " "	+ 0.0025 c.c. serum)	=0
" "	+	" " "	+ 0.002 c.c. serum)	=0
" "	+	" " "	+ 0.00175 c.c. serum)	=0
" "	+	" " "	+ 0.001425 c.c. serum)	=0
" "	+	" " "	+ 0.001225 c.c. serum)	=0
" "	+	" " "	+ 0.00111 c.c. serum)	=0
" "	+	" " "	+ 0.001 c.c. serum)	=0
" "	+	" " "	+ 0.0005 c.c. serum)	=0

I was very anxious to determine how much less than this quantity would inhibit the coagulating power of the rennet. But at this point my experiments were interrupted by pressure of other work and the matter was dropped for several weeks. When I was able to return to it again, I found that what Morgenroth had discovered regarding the instability of the antirenene was correct, and that my serum had entirely lost its power, either when added to the milk or when added to the rennet, to interfere with coagulation.

SUMMARY.

The experiments confirm Morgenroth's discovery that the repeated introduction of rennet is followed by the formation of an antibody inhibiting its action. They show that properly prepared mixtures of rennet and antirenene give a specific precipitate, and show, I think for the first time, that the action of the antirenene is infinitely more active when the two are mixed and allowed to stand for some time before being added to the milk than when immediately added to the milk.

This is in thorough keeping with what was observed by Martin and Cherry regarding the interaction of venom and antivenene. I am also able to confirm Morgenroth's observation of the instability of the antibody.

DISCUSSION.

Dr. Joseph McFarland, Philadelphia—After the use of the chloretone in the milk I found that I was able to keep the milk as long as I liked. Owing to the negligence of the attendant in not cleaning up the bottles on the stand in my laboratory some of them stood for eight weeks without contamination. The milk simply dried up. I have found chloretone one of the best reagents for the preservation of serums, milks, urines and organic extracts from bacterial contamination. Bacteria will not grow in any of these when the chloretone has been added and there is no injurious chemical action.

Dr. L. Hektoen, Chicago—I would like to inquire whether the rabbit serum has any coagulative power.

Dr. J. W. Foss, Phoenix, Ariz.—Will anything short of a saturated solution of chloretone act as a preservative?

Dr. Joseph McFarland, Philadelphia—Replying to the first question, normal horse serum contains a body that slightly inhibits the coagulative power of rennin, but rabbit serum does not.

As to the chloretone, I always use the saturated solution because that is the easiest to prepare.

THE PROTOPLASMIC ACTIVITY OF THE RENAL EPITHELIUM,

AS DETERMINED BY THE ELIMINATION OF PIGMENTS INJECTED INTO THE CIRCULATION.

WM. S. CARTER, M.D.
Professor of Physiology, University of Texas.
GALVESTON, TEXAS.

INTRODUCTION.

The question of the functional activity of the renal epithelium is ever one of deep interest, both to the physiologist and to the pathologist.

It will be remembered that Bowman's theory concerning the separation of the urine by the kidney was originally founded on anatomic findings entirely and not on experimental evidence. According to this view, the glomeruli separate the watery portion of the urine and the freely diffusible substances, while the specific ingredients of the urine, viz., the urea, uric acid, etc., are secreted by the cells of the uriniferous tubules.

Bowman's theory was replaced for a time by that of Ludwig when the latter investigator and his school showed the close relationship which exists between the circulation of blood in the kidney and the amount of urine separated. This theory held that the separation of urine by the kidney is purely a physical process, the blood-pressure in the glomerular capillaries causing all the ingredients of the urine to filter through into Bowman's capsule in very dilute solution. During the passage of this dilute solution down the uriniferous tubules the water was supposed to diffuse back from the urine into the lymph, so that the urine becomes more concentrated as it enters the pelvis of the kidney.

Further investigation of the subject soon showed that alterations in the general arterial blood-pressure do not always cause corresponding changes in the amount of urine formed, while the latter may be influenced by conditions which do not affect the former. These facts called the first part of Ludwig's theory seriously into question. The latter part, pertaining to the diffusion of water from the uriniferous tubules into the lymph, was demonstrated to be impossible, as the urine has a greater osmotic pressure than the lymph, and if any diffusion takes place, the water would pass in the opposite direction to that contended by Ludwig.

Heidenhain then put forward a theory which is in part a revival of Bowman's hypothesis in that the specific ingredients of the urine are held to be secreted by the protoplasmic activity of the cells lining the uriniferous tubules. Heidenhain went still further and held that the water and freely diffusible constituents of the urine are secreted by the flat epithelium covering the glomeruli and that these are not merely filtered by a physical process alone, although the influence of changes in the general or local circulation on the flow of urine is fully recognized.

Both of these theories have been modified from time to time, and while there may be minor differences, there are two main views held at the present time as to the functional activity of the kidney:

(1) *The Filtration-Absorption Theory* or *Modified Ludwig's Theory.*—This holds that all the ingredients of the urine in very dilute solution are filtered through the capillary wall and the epithelium covering the glomerulus, and that the water and chlorids are absorbed by the cells lining the uriniferous tubules, while the urea, uric acid, phosphates, sulphates, etc., pass on to the pelvis of the kidney in more concentrated solution.

According to this view, the epithelium of the uriniferous tubules is not excretive, but is only concerned in absorption. These cells are supposed to have a selective power in absorbing certain ingredients like the chlorids, while other diffusible substances like urea pass on. If this theory be correct, Heidenhain calculated that fully 70 kilos of water must filter through the glomeruli daily.

(2) *The Excretory, Vital,* or *Bowman-Heidenhain Theory.*—It is contended by those who hold to the other explanation of the function of the kidney that only the water and inorganic salts are separated by the glomeruli. The glomerular epithelium is supposed to be permeable to certain substances and not to others, so that the fluid which collects in the capsule of Bowman contains the inorganic salts in the relative proportion in which they occur in the urine. The cells lining the tubules, and especially those of the contorted tubules, are held to separate the specific ingredients of the urine by an excretory action, i. e., by a protoplasmic activity similar to the secretory activity of other glands.

The main point at issue between these diverse views is whether the renal epithelium is absorptive like that lining the intestine, or excretory in function. If the former is correct, then water and salts are absorbed from the urine into the lymph; if the latter is correct, then the metabolites and possibly some of the salts of the urine are separated by protoplasmic activity from the lymph into the urine as it passes down the tubules.

In trying to determine which of these theories is correct most of the work in recent years has been carried on by studying the molecular concentration of the urine under different conditions and comparing it with that of the blood. Much has also been done in studying the action and elimination of different salts.

Unfortunately, there is no ingredient of the urine which can be traced through the renal epithelium by microchemical methods. Bowman[1] and Von Wittich[2] described the presence of uric acid crystals in the epithelial cells lining the uriniferous tubules of birds, but it has since been contended by Schmidt[3] that these observations are incorrect, and that uric acid crystals only occur within the lumen of the tubule and on, but not within, the protoplasm.

Heidenhain[4] made use of a soluble stain which can be injected into the circulation without any harm and can be precipitated in the kidney by perfusing it with absolute alcohol. Sodium sulphindigotate (indigo carmine), when injected into the circulation, appears in the urine in from 2 to 3 minutes. Heidenhain found that if the kidney be quickly excised 5 minutes after the injection of the stain and perfused with absolute alcohol, the pigment is precipitated chiefly in the medulla of the kidney. When the spinal cord was cut prior to the injection so as to lower the blood-pressure and thereby stop the flow of urine, he found the pigment chiefly in the cortex and on microscopic examination found the precipitated pigment granules principally within the lumen of the convoluted tubules, and to a less extent in the epithelial cells lining them.

Heidenhain concluded from these experiments that this pigment is eliminated by an excretory activity of the cells lining the convoluted tubules. While it does not necessarily follow from this that urea is excreted in the same way, nevertheless, this would seem highly probable from the large proportion of this metabolite in the urine if such excretory activity can once be positively established.

Other experimenters have not always obtained the same results from injecting indigo carmine that Heidenhain did. The results obtained with this dye are extremely variable, but admitting that they are uniform,

---

1. Bowman: Phil. Trans., London, 1842.
2. Von Wittich: Arch. f. mik. Anat., 1875, Bd. xi.
3. Schmidt: Arch. f. d. Ges. Physiologie, 1890, Bd. xlviii.
4. Heidenhain: Hermann's Handbuch d. Physiologie, vol. v.

quite a different interpretation has been placed on them. The pigment precipitated in the kidney has been found to occur chiefly in the lumen of the uriniferous tubule and in that part of the renal epithelium which immediately borders on the lumen. It does not occur in such abundance in these cells toward the basement membrane. It is contended by some[5] that the presence of these granules in this part of the cell might be due to absorption from the urine within the tubule as readily as to excretion from the lymph into the urine. This view is rendered more plausible by the fact that by varying the conditions of the experiments the glomerulus is often found to be stained.

PLAN OF EXPERIMENTATION.

The experiments presented in this paper were undertaken with the idea of attempting to clear up this point, viz., whether the protoplasmic activity of the renal epithelium is concerned in absorption or in excretion in the elimination of pigments injected into the systemic circulation.

Different methods were used to stop the free flow of urine with the idea of diminishing the amount of water separated by the glomeruli without interfering with the protoplasmic activity of the epithelium lining the tubules. In one experiment the spinal cord was cut so as to lower the blood-pressure and thereby stop the flow of urine. In two others advantage was taken of the anuria from surgical shock. It is a matter of common experience in performing experiments on the kidney that often the urine does not flow for a considerable time after a kidney or ureter has been exposed, and at times it is necessary to inject a diuretic or physiologic salt solution to establish the flow. As the amount of pigmentation of the kidneys varies in different animals considerably, even when the conditions of experimentation are identical, it is obviously desirable to stop the flow from one kidney without interfering with its circulation, while the other one continues to act normally. This is far preferable to the method of stopping the flow in both kidneys, as it allows comparison in the same animal.

---

[5] Starling: Schäfer's Text-book of Physiology, vol. I.

In three experiments one renal artery was compressed between the fingers for one-half to one minute at a time and repeated if necessary. This usually causes a temporary cessation in the flow of urine without interfering with the blood supply, as no injury is done to the artery. Unfortunately, when fluids are subsequently injected the flow of urine sometimes starts again, but is never as great as on the normal side.

In eight experiments the ureter of one side was connected with a mercury manometer by means of a cannula and the urine allowed to flow until the mercury in the manometer ceased to rise. It requires a pressure of 30-40 mm. Hg. to stop the flow of urine. In this way the ureter and pelvis are distended and the outflow from the uriniferous tubules is thus obstructed and comes to a standstill. Normally the pressure in the ureter necessary to stop the flow of urine does not exceed 40 mm. Hg., but under the influence of diuretics it may go as high as 60 or 70 mm. of Hg.

Several of my experiments were performed before the publication of Cushny's paper[6] on the elimination of salts by the kidney when the ureter is obstructed, and until then my attention had not been called to the interference with the renal circulation by obstructing the ureter. Lindemann[7] showed that a pressure of 100 to 200 mm. of Hg. in the ureter causes the kidney to swell up and interfere seriously with the renal circulation, as the outflow of blood from the renal vein is greatly diminished, but if this pressure does not exceed 50 mm. Hg. the venous outflow is not reduced by 10 per cent.

---

[6] Cushny: Brit. Journ. of Phys., vol. xxviii, No. 6.

[7] Lindemann: Beiträge z. path. Anat. und Phys., xxi, p. 500, 1897.

In my later experiments a T cannula was tied in the obstructed ureter after a method devised by Cushny, so that one arm could be connected with a manometer, while a short piece of rubber tubing on the other arm, with a screw pinch cock, allowed the urine secreted under pressure to escape and in this way the pressure was kept uniformly between 35 and 40 mm. of mercury.

An effort was made to see if the protoplasmic activity of the renal epithelium could be lessened by atropin. It is supposed by some that this alkaloid checks the renal activity in the same way that it does that of most other glands. Careful urea determinations were made of the urine collected from the ureters for five-minute periods before and after the administration of atropin in three experiments, but there was no diminution in the quantity of urine or of urea, although the flow of saliva was completely stopped and could not be excited in any way. Pilocarpin also fails to increase the amount of urine or of urea.

SELECTION OF A SUITABLE PIGMENT.

Experiments with sodium sulphindigotate (indigo carmine) are so extremely variable that satisfactory results were never obtained, although it has been tried in nine experiments not included in this paper. Care was taken to repeat exactly the conditions as described by Heidenhain, but the trouble seems to lie in the composition of the pigment and the change which it undergoes under the influence of the living tissues. The living cells appear to reduce it to a colorless substance. This change is so great that even though the kidney is colored blue when it is first cut out and perfused with absolute alcohol, it soon loses color, and sections mounted from it show no color granules. The pigment was the purest obtainable from different sources, but the results were always the same, even though large amounts were injected (5 c.c. to 7.5 c.c. of saturated solution per kilo of body weight).

Starling[5] recommends the use of carmine dissolved in a weak solution of sodium hydroxid. Carmine has the advantage of being more complex in its composition and less diffusible, so that it can be traced through the tissues more readily. It is also very much more stable; is not reduced by the tissues, and can be more completely precipitated by absolute alcohol than can indigo carmine.

The only disadvantages of carmine are its comparative insolubility and the effect of the sodium on the circulation. A saturated solution in weak NaOH solution rarely contains more than 1 per cent. of carmine, and may contain much less if made hastily. When such a solution is rapidly injected directly into the vein it causes the heart to beat slowly and a fall of pressure ensues. This can be obviated by making the injection slowly, and with this precaution from 5 c.c. to 7 c.c. of a saturated solution of carmine in 0.1 per cent. NaOH may be injected for each kilo of body weight. It is very essential that the solution be freshly prepared, as it decomposes very readily.

To avoid the effect on the heart of any free alkali, commercial sodium carminate was tried, but proved less satisfactory than a fresh solution of carmine. The tissues were not so deeply stained and the stain was more diffuse and not so completely precipitated by absolute alcohol.

Sometimes when carmine has been injected into the circulation the urine and kidneys remain remarkably free from the pigment, although the other tissues are stained and the blood-pressure has remained normal throughout. This caused us to try other materials which can be used for the microchemical examination of tissues.

As large amounts of potassium ferrocyanid can be injected directly into the circulation without any injurious effect, this salt was used, and after it had appeared in the urine the kidneys were excised and perfused with a weak solution of ferric chlorid containing a little free

HCl. The entire organ turned blue after a time, but sections showed a diffuse stain in some places, with deeply stained material in the lumen of the straight tubules. The results were less satisfactory than those obtained with carmine.

The injection of a soluble salt of iron (citrate of iron and ammonium) was next undertaken, and after the iron had been found in the urine for some time the animal was killed. One kidney was then perfused with a weak solution of ammonium sulphid, and the other was cut into very thin pieces and placed in a weak solution of potassium ferrocyanid acidulated with HCl. The kidneys showed marked precipitates of black in the one kidney and blue in the other, but microscopic sections of the organs were not as satisfactory as those made from experiments in which carmine was used.

Recently a freshly prepared liquor carmini (U. S. P.) has been used. This is a 6.5 per cent. solution of ammonium carminate from which all free ammonia has been driven off by gentle heat or gaseous diffusion. It has the advantage that it contains much more carmine than is possible to get in solution otherwise, and does not lower the blood pressure if injected slowly. It has the disadvantage over a solution of sodium carminate that it increases the flow of urine, probably in the same way that saline diuretics do, as it contains 35 per cent. of glycerin. This also causes a more diffuse staining of the glomeruli than is seen after the injection of the other pigments, although two parts of physiologic salt solution were added to the liquor carmini for injection. At first 5 c.c. or 6 c.c. of liquor carmini per kilo of body weight were injected, but this causes such diffuse pigmentation that 4 c.c. per kilo is a better proportion. Less than this does not give such good results.

In the experiments with carmine and indigo carmine the kidneys were perfused with absolute alcohol through cannulæ tied in the renal arteries. At first this was done with a syringe, but it was found much better to make the injections by gravity, using a separating funnel at a height of about six feet and allowing the absolute alcohol to perfuse for an hour, the kidney being covered with alcohol. The alcohol flowed freely from the renal vein and some escaped from the ureter. The organ was then cut open and thin pieces were placed in a large excess of absolute alcohol. These were then imbedded in paraffin and mounted unstained, so that none of the pigment could diffuse out.

When comparisons were made between the two kidneys the cannulæ of the two renal arteries were connected by a Y tube with one column of alcohol, so that the pressure and amount of absolute alcohol perfused were as nearly equal as is possible to obtain.

In precipitating the iron and potassium ferrocyanid in the kidney the precipitating solution was perfused by gravity and the tissues were then fixed by absolute alcohol and mounted in the same way.

One important fact to remember in this connection is that the vasa recta (i. e., the arterial twigs running between the straight uriniferous tubules) receive much more alcohol when the kidney is perfused than the capillaries about the convoluted tubules. I have determined this definitely by injecting a gelatin mass colored with soluble Prussian blue, with exactly the same pressure and conditions used for perfusing with alcohol. The kidney was warmed by perfusing with physiologic salt solution at 40 C. and it was kept covered with the same. When the gelatin was perfused it flowed freely from the renal vein and the pelvis and ureter were colored blue. The gelatin was then made to set by plunging the kidney in very cold physiologic salt solution, while the pressure in the renal artery was kept up.

On section the blue was found chiefly in the vessels between the straight tubules, in the interlobular arteries and in the capillaries of the glomeruli, but not in the second set of capillaries (renal portal capillaries) about the contorted tubules. This may account for the more complete precipitation of pigment in the straight tubules, and especially just at the junction of the cortex with the medulla. It is here that the greatest amount of pigment is found precipitated in these experiments.

THE ELIMINATION OF THE PIGMENT.

Indigo carmine, potassium ferrocyanid or carmine may be detected in the urine flowing from the ureter in from two and a half to three minutes after it has been injected into the jugular vein. In the case of iron it requires a slightly longer time—from four to five minutes. The tissues are all diffusely stained after the injection of carmine or indigo carmine. When the kidney is cut open after it has been perfused so as to precipitate the dye, it is seen to be deeply colored, mostly in the medulla and where the latter joins the cortex. On section most of the pigment is found within the uriniferous tubules. The question at once arises, is this pigmentation merely the result of diffusion, or is this foreign substance eliminated by the kidney and gotten rid of in this way?

In the case of carmine it can at once be stated that this is an excretory activity and not merely a diffusion. This statement is based on the observation that pigment granules can be seen within the epithelial cells of the organs of excretion, viz., the kidney, liver and colon, while we do not find them in the cells of the pancreas, spleen or muscles. When moderate amounts of the pigment have been injected these granules do not occur in the cells lining the stomach or small intestine, although the vascularity of all these tissues is fully as great as that of the excretory organs. Furthermore, the contents of the colon and sigmoid flexure show the presence of the dye, while the contents of the stomach and small intestine are not colored unless very large amounts of carmine have been injected. Sections of the tissues not concerned in the elimination of the stain show the pigment granules within the blood-vessels and perivascular lymph spaces, but not within the cells of the parenchyma.

THE MANNER OF ELIMINATION BY THE KIDNEY.

Attention may next be directed to determining whether the elimination by the kidney is the result of filtration through the glomeruli or the result of a protoplasmic activity of the epithelium lining the uriniferous tubules. Neither one of these processes precludes the possibility of the other, and both may operate at the same time. This is often lost sight of by those who endeavor to prove a favorite theory.

When a kidney is removed one-half hour after the injection of carmine into the systemic circulation; is perfused with absolute alcohol for an hour in the manner before mentioned, so as to fix the cells and precipitate the stain *in situ;* and is then imbedded, sectioned and mounted in agents which can not dissolve the stain, most of the pigment is found in the straight tubules of the medulla and those of the medullary rays reaching from the medulla into the cortex. The convoluted tubules of the cortex contain less pigment and it only occurs in places while the glomeruli are quite free from it.

The precipitated carmine occurs chiefly in the lumen of the convoluted tubule and in that part of the epithelial cells which borders on the lumen. The part of the epithelial cells which is nearest the basement membrane is not free from pigment, but with the low power appears to be uniformly tinted.

As stated before, this condition is taken to indicate absorption by those who hold to the filtration theory, while it is interpreted as evidence of excretory activity by those who hold the Bowman-Heidenhain theory.

The experiments presented in this paper seem to indicate that these granules are in the process of excretion rather than of absorption. This view is based on the following facts:-

1. The pigment in the renal epithelium of the contorted tubules is found chiefly, but not exclusively, in the

part bordering on the lumen. If these cells be examined with a high power (1/12 oil immersion lens), the basal part shows not only a diffuse stain, but fine carmine granules. These can be found not only in cells containing large granules, but in many cells in which there are no coarse granules near the lumen. The difference in the size of these granules is fully as marked as the variation in the size of the neutrophile and eosinophile granules of leucocytes. Why is there this difference in the size of these precipitated carmine granules?

It has been pointed out that in perfusing the kidney with a pressure sufficient to cause a free flow from the renal vein, the vasa recta and the interlobular arteries receive most of the perfused fluid, while the capillaries about the convoluted tubules receive very little. Some of the perfused fluid filters through the blood-vessels of the glomeruli and escapes from the uriniferous tubules into the ureter even when absolute alcohol is used. It would seem possible, therefore, that the pigment is more completely precipitated in the straight tubules and outer part of the convoluted tubules than in the basal part of the latter. This would only explain the difference in the size of the granules, but not the difference in the amount of pigment in these two parts of the cells lining the contorted tubules.

This difference in the distribution of the pigment does not necessarily indicate that it is absorbed by these cells. It will be recalled that in the mammary gland during active secretion the fat globules accumulate in that part of the cell next to the lumen of the acini, and are not uniformly distributed in the part near the basement membrane. The same thing is true of the zymogens of most glands which pour out external secretions. No one would contend from this condition alone that these products of gland activity are absorbed and not secreted.

2. Against the view that these pigment granules are being absorbed, we would point to the fact that some

cells in the liver and many cells in the colon show the presence of such granules. If the amount of carmine injected is very large this pigment is also found in the epithelial cells lining the stomach and intestine, but when moderate amounts are used the dye is excreted chiefly by the kidneys and colon. The contents of these hollow viscera show that the carmine is excreted. Other tissues such as the pancreas and spleen, which are just as vascular, do not show the carmine granules in the cells. It can not be contended that the carmine granules in the cells lining the alimentary tract are being absorbed. It is much more probable that the epithelial cells of the uriniferous tubules like those of the colon are active in excreting this foreign substance from the blood.

3. If the ureter be obstructed so that the outflow of urine is stopped without interfering with the circulation of the kidney, the renal epithelium is free to act while the separation of fluid by the glomeruli is reduced to a minimum. When carmine is injected under these circumstances the amount of pigment in the obstructed kidney is much greater than in the normal one. The cortex is more deeply colored than in the unobstructed kidney, but still contains less than the medulla. Sections show most of the pigment in the lumen, as very little is flushed out. The amount of pigment in the cells of the contorted tubules, and especially toward the basement membrane, is relatively increased. It might be contended that this is due to increased absorption under pressure, but the concentration of the urine which accumulates in the pelvis of the kidney when the ureter is obstructed argues strongly against the view that a dilute urine continues to be actively separated by the glomeruli when the ureter is obstructed. This has been determined by comparing the amounts of urine and urea respectively given off by the normal and by the obstructed kidney. My own experiments are not in accord with those of Cushny on this point.

3. When the free flow of urine is stopped by cutting

the spinal cord and thereby lowering the blood-pressure, or as the result of surgical shock, or as the result of compressing the renal artery for a short time without injuring the intima, the injection of carmine into the circulation results in far more of this pigment being found in the uriniferous tubules and in the cells lining them than could be accounted for by a slight transudate which might continue from the glomeruli with complete resorption of the water. Indeed, when the flow of urine has been stopped on one side by the temporary compression of the renal artery the kidney of that side shows fully more carmine than its fellow. This condition would be reversed if the carmine in the cells were the result of absorption from a dilute urine.

4. In none of these cases does the stain show extensively in the glomeruli or capsule of Bowman when carmine dissolved by weak sodium hydroxid has been used. Even when the ureter has been obstructed and the kidney is deeply pigmented as contrasted with its fellow, the glomeruli do not show the pigment granules one would expect to find if the filtration through these structures had continued. If all the pigment found in the uriniferous tubules had come from the glomeruli and none from the epithelial cells, then the glomeruli should also be stained when their activity is stopped by obstruction to the outflow of urine from the kidney.

When ammonium carminate held in solution by glycerin is used the glomeruli show carmine granules, whether the ureter is obstructed or not. This solution has a greater diuretic action than any other substance used, and it is probably in more complete solution and more diffusible than the carmine dissolved by soda.

5. The glomeruli do not show a deposition of carmine granules, even when the animal is killed shortly after the injection of carmine dissolved by sodium hydroxid. In one experiment the kidney was excised four minutes after the injection of carmine and one minute after it appeared in the urine; in others after intervals

of 10, 15 and 20 minutes, but in none of them have the glomeruli been stained as has been described with indigo carmine.

In conclusion it should be stated that these experiments merely indicate that pigments are excreted by a protoplasmic activity of the renal epithelium. They do not contend that none of the pigment is filtered through the glomeruli. On the other hand, when ammonium carminate is used the sections indicate that this is the case, and Starling's experiments with indigo carmine show the same thing. As stated before, we should bear in mind that both processes may operate at the same time.

The elimination of pigments by the kidney does not afford a method of determining positively and finally whether the rodded epithelium is excretive or absorptive in function, but the former seems the more probable. Of course, urea and the metabolites of the urine may be handled in a different way from foreign substances injected into the circulation. However, it seems improbable that the cells lining the uriniferous tubules are concerned exclusively in absorption, as has been contended recently.

DISCUSSION.

Dr. E. R. LeCount, Chicago—I would like to ask if the arrangement of the pigment granules in the secretory cells of the convoluted epithelium was in rows, at right angles to the channel. We can recall that in various kinds of secretory epithelium it has been proven that there are intracellular passages. In the pancreas, liver cells and others there are pathways which lead into the channels. The renal epithelium is striated and the striations are at right angles to the tubules. I do not know that it has been proven that this is due to the existence of passageways, but it would be interesting to determine that point.

Dr. W. S. Carter, Galveston, Texas—I have not observed any such arrangement. The coarse pigment granules occur in great numbers near the lumen of the tubule, and where we have these very fine ones they are very evenly distributed through the protoplasm.

THE INFLUENCE OF CONSANGUINITY ON THE ORGANS OF SPECIAL SENSE.

LEE WALLACE DEAN, M.S., M.D.
IOWA CITY.

In treating this subject I have found that I am compelled to confine myself almost entirely to the eye. It presents to us such possibilities for exact investigation that the results secured overshadow those gained from a study of the other organs of special sense.

We have here blood vessels and a nerve with its end organ exposed to view. We can look on mesoblastic and epiblastic tissue. We can observe embryonic conditions if they exist. With the exception of the nervous system, more degenerate conditions are found in the eye than in any other part of the body. As most of the deleterious results of consanguinity are degenerative conditions, we ought to expect this to be a good field for research. You will readily observe that this paper is not a complete treatise on this subject. It has been almost impossible to find literature relating to it. I can only give to you the results of three years of observation of cases and study of them.

It is entirely unnecessary to go into the question as to the influence of consanguinity on organism as a whole. Talbot very nicely answers this question when he says that if the parent stock is perfectly pure there can be no bad results from consanguineous marriage. But if the parent stock is not pure there may be serious consequences. It is so rare to-day to find a perfect parent stock. An apparently perfect stock may not be so because hereditary influences may be quiescent for generation after generation, as is shown by atavism. In order to bring before you the practical side of this subject and its economic importance, I wish to cite some cases. All cases where the name of the observer is not mentioned are cases that have come under my own observation unsolicited in the short space of three years. Some of these cases were reported to the American Academy of Opthalmology and Rhinolaryngology:

Case 1.—Male, age 17. Parents, grandparents, uncles and aunts had no serious eye trouble or degenerate stigmata. Parents were bright, well-to-do people. He has three sisters, Bessie, age 15, who is partially blind; Effie, age 9, whose vision is good, and Grace, age 4, who is blind. He has three cousins, one boy and two girls, all in the same family. Of these, Louis, age 16, is almost blind; Oran, age 19, can not count fingers, and the girl, age 13, seems to have unimpaired vision. The trouble in each case was retinitis pigmentosa. The fathers of the two families were brothers and the mothers sisters, and the fathers were cousins of the mothers. As the result of these two marriages we have in one family four children, three of whom are partially blind, and in the other family three, two of whom are practically blind.

Case 2.—Female, age 14. Father and mother have brown hair. Parents were related. There is no history of malformation or other degenerate stigmata in the family. The girl is very large, but weak; she is not intelligent. Her hair is white; iris is a light blue. Examination of eyes revealed nystagmus, V.=6/24. Fundi without pigment. Diagnosis, albinoism.

Case 3.—Female, age 16. Parents second cousins. Patient's teeth were imperfect. She had but three upper incisors, one root germ not having developed. An examination of eyes revealed V.=fingers in 2 M. Her eyes are so small that she has to hold her lids open with her fingers in order to see. On the right side there is a congenital absence of the iris. In the left eye the cornea is elliptical, being 3 mm. wide in a horizontal direction and 2 mm. in a vertical direction. On this side there is a large coloboma of the iris, one-half of the lower portion being absent.

Case 4.—Male, age 17. Parents are perfectly healthy. None of his ancestors have shown any signs of degeneracy so far as could be learned. His father and mother were first cousins. He has one brother and two sisters. One of his sisters is an idiot. She has microphthalmos, misplaced ears and other signs of facial degeneracy. The patient is exceedingly simpleminded. His ears are large and placed at right angles to the head. The helix is deformed. His face is covered with a growth of silky hair. The lower jaw is exceedingly small and is retrusive. He has no adenoids, but always keeps his mouth open. Examination of the eyes reveals on the right side a microphthalmic eye with a coloboma of the iris and choroid. On the left side there was an apparent absence of the eye. There were two small lids and a socket. No eye could be felt by introducing the finger in between the lids and feeling about in the orbit. The lower part of the socket was deformed. The union between the malar and the superior maxillary bone had never taken place. There was a space one-fourth of an inch wide between the two bones. The patient was given an anesthetic and a dissection of the contents of the orbit was made. The fissure between the malar and the superior maxillary bone was found to extend back to the spheno-maxillary fissure. In the apex of the orbit, lying closely against the optic foramen, was found a rudimentary eye. It was removed. It was about one-third of an inch in diameter. With the naked eye no change indicating the cornea could be detected. The eye was hardened in formaldehyd and alcohol and stained with hematoxylin and eosin. The eye was composed of an outer thick fibrous coat. The cornea could only be differentiated microscopically from the sclera by the absence of an inner lining of pigmented cells. The eye was filled with a myxomatous tissue much more solid than the normal vitreous. It contained some blood vessels, one of which was very large. No trace of retinal elements could be found. The internal structures seemed to have all undergone a myxomatous and mucoid degeneration. The lens and retina seemed to be absent.

Case 5.—This is not a single case, but the report of a family with six children. The father and the mother were both dark complexioned. There was no history of any degenerate condition in the family. They were first cousins. They had but six children. Of these, two were dark complexioned and had good vision. The other four were albinos and had a vision of 6/12 or less.

Case 6.—Female, age 5. Parents were first cousins. No history of any serious eye trouble or of degenerate conditions in family. Child was very dull. Left eye began to enlarge shortly after birth. O. D. apparently normal. O. S. very much enlarged. Tension normal. Diagnosis, congenital glaucoma left. The left eye was enucleated. The usual cupping of the disc was present. Microscopic examination failed to reveal any obstruction of the canal of Schlemm.

Case 7.—Female, age 6 months.. This case I saw in consultation with Dr. Cooling of Wilton Junction, Iowa. Parents were healthy. No history of any tumor or eye trouble in the family could be elicited. Parents were first cousins. The parents said that two months before the right eye began to increase in size and a few weeks later the left began. The child apparently could not see. Pupils were dilated; would not react to light. Tension in right eye +2, and in the left +1. Both eyes were enlarged, the right the more. Lying behind the iris in each eye could be seen a large tumor. Diagnosis, double-sided neuroepithelioma. Four months after the child was seen it died.

Case 8.—Male, age 4. Parents' and grandparents' history negative. Parents cousins. Boy has congenital coloboma of iris in each eye and anterior polar cataract in the right eye.

Case 9.—This is a family reported by Dr. Vail. Parents cousins. Consanguinity was positively denied for a year. Parents' and grandparents' history negative. As the result of the union seven children were born. Five had congenital cataract. The cases were so helpless that Dr. Vail recommended that no more children be born.

Case 10.—Dr. Alt reports a family in which there is constant intermarriage. Senile cataract is hereditary in the family. In the last generation several cases of congenital cataract have made their appearance. If there is any relation between the senile cataracts and the congenital the former must be hereditary cataracts not the result of a sclerosis of the nucleus of the lens, but rather a nutritive disturbance. One could not think of the former condition appearing in children.

Case 11.—Female, age 12. Parents' history negative except that they were first cousins. Is an only child. Has simple atrophy of the optic nerve.

Of 181 blind children in the Iowa College for the Blind in 1900, 9, or about 5 per cent., were the result of consanguineous marriage of the first degree. The number of consanguineous marriages of the first degree in Iowa is far below 0.5 per cent. I ought to say that it is exceedingly difficult to secure a history of consanguineous marriage when present. There were probably others present in the college the result of consanguineous union.

If we exclude from the list those blind children who were blind because of blennorrhea neonatorum, sympathetic ophthalmia, trachoma, etc., and consider only those who suffered because of congenital conditions, we would find that 14 per cent. were the result of consanguineous marriage of the first degree. These figures seem large. I do not think they ought to be considered as indicating the relative proportion of degenerate eyes in families the result of consanguineous marriage and in those not, because we are considering here only one field. Among the pupils who have entered the college since 1900 the per cent. is about the same.

Two factors may enter into the production of many of these conditions: 1. The eye is really an outgrowth from the brain, and is consequently subjected to the same conditions as the central nervous system during its development. 2. The eye is changing, and an organ that is adapting itself to new conditions is more liable to malformation than one with a constant condition. The socket is becoming less deep and the superciliary ridges less marked. Fuchs believes that in families with school myopia the eyes have adapted themselves to their work.

A number of interesting things are suggested by these cases: 1. The relation of the inheritability of a condition to its production by consanguineous marriages. I would judge from these cases that the greater the inheritability of a condition the more liable is it to be the result of consanguineous marriages. Theoretically, this would also be the case. Retinitis pigmentosa is a disease of great inheritability. I have now under observation a grandfather, a mother and a son each with retinitis pigmentosa. As it is a comparatively rare condition there is not the chance for doubting the tendency of its appearing by marriage of individuals not related as the more common conditions.

The influence of consanguinity on retinitis pigmentosa has been mentioned by several. Dr Liebreich says that of 26 cases of retinitis pigmentosa, 53.8 per cent. were the result of consanguineous marriage. Magnus reports 33 per cent. of cases of retinitis pigmentosa in children, the result of consanguinity. Of 66 cases reported by Chapault, 45 per cent. were the result of consanguineous marriage. Of 18 cases under my observation where the history of the parents could be secured, 8, or 44 per cent., were the result of consanguinity. Schobel[1] says it is generally dependent on consanguinity. A very careful examination into the history of the ancestors of the cases I mentioned failed to reveal any eye trouble of importance. Yet in the first group mentioned we have these cases appearing by intermarriage in the two groups when consanguinity took place. Albinoism has a strong inheritability. Congenital cataracts have also strong inheritability. Most of the cases mentioned were not true cataracts, but capsular opacities, the result of non-absorption of fetal structures. In approximately one-third of the cases, however, the capsule was not opaque, but the lamellæ were affected.

Some light may be shown on the cases reported by Dr. Alt, where congenital cataracts appeared in the offspring of relations suffering from senile cataract by the fact that hereditary cataracts some time appear earlier in each succeeding generation. I know of a case where the grandfather developed cataracts at about 50; the mother had one at 35, and the son had congenital cataracts.

2. It is interesting to note that where there is an arrest in development, as in the cases of microphthalmos, coloboma of the iris, congenital cataract, and anophthalmos, the eyes are in an opposite state to those of eyeless fishes and worms where they have been lost by disuse. Wagenmann[2] has found that the lens and the retina were almost the least of the structures acted on, and that the phyletic degeneration does not follow the reverse order of development. The eye does not resemble part embryonic conditions as in the eyes where there is an arrest of development. At birth the eye is almost normal, but with age it degenerates. The microphthal-

---

[1] System of Diseases of the Eye. Norris and Oliver, vol. iii, p. 460.

[2] Archiv für Entwickelungs Mechanik der Organismen, 8, 4.

mic eye improves the first ten years after birth, owing to a diminution of the hyperopia. A third point in connection with these cases is the resistance after operative procedures. Dr. Gruber of London writes me that he has operated on a number of such eyes with good results. I have never seen any serious sequelæ following an operation. While there is an arrest of development, the nutrition is apparently normal.

As to the influence of consanguinity on the neuro-epithelioma, I would certainly not express any opinion. I simply mention the case as I found it while conducting my investigations.

DISCUSSION.

Dr. J. W. Foss, Phoenix, Ariz.—This subject of inbreeding is given a great deal of attention by stockmen, but is neglected by human beings. About two months ago I visited an ostrich farm near Phoenix, and they had just hatched out eight or ten chicks, and out of the lot, because of physical deformities, there was only one it was possible to save. This was the result of interbreeding. It costs so much to get a male ostrich from Africa that to save expense they interbreed and get few perfect offspring as a result. This paper gives us the key to our duty as physicians, and we can prevent many of these consanguineous marriages by firmly and persistently impressing on our patients and friends the unfortunate results of such union.

PRECISION IN THE DETERMINATION OF HUMAN PARASITES.

HENRY B. WARD, Ph.D.
LINCOLN, NEB.

The ectoparasites of man are, generally speaking, well known, and many of them have been recognized from the earliest times. They are also easily determined, in the main, while, on the other hand, the difficulties to which they give rise are not, as a rule, serious, but yield readily to simple treatment. With the endoparasites, however, the case is precisely the reverse. They are not, as a rule, more than superficially known, and it is only recently that attention has been generally called to their number and the effects often serious which they produce in the human organism.

To be sure, a long series of such forms has been recorded in the past, and the serious effects of their parasitism has been emphasized in some quarters. Thirty years ago Leuckart[1] listed thirty-three species which had been found in man, and, in company with Virchow and a long list of other investigators, called repeated attention to the deleterious effect certain species exert. Braun's more recent work[2] discusses of certain and doubtful species 15 *Trematoda,* 20 *Cestoda* and 38 *Nematoda,* besides 30 to 40 *Protozoa,* which have been recorded from the human host. In studies on the various groups which I have recently published[3] this list is increased by two species, although the interval between the publication of Braun's lists and mine is not a year.

---

[1] Leuckart, R.: Die Parasiten des Menschen, 2 vols., Leipzig, 1876.

[2] Braun, M.: Die tierischen Parasiten des Menschen, 3 Aufl., Leipzig, 1902.

The various studies, however, have chiefly been made on forms found in the old world. Within very recent times these studies have begun to be extended over other lands. All the new forms recorded during the last five years have been extra-European, either new species peculiar to other lands, or new regions within which known forms have been found to exist. Perhaps the greatest advance has been in knowledge of the geographical distribution of human parasites. The large number of isolated cases of the occurrence of certain species has been supplemented by other cases showing more general occurrence or wider distribution, the results of which have been to demonstrate that these parasites are far more common and widely distributed than was believed heretofore. The accompanying table, which lists all human parasites of the various groups of worms heretofore recorded with a statement of the regions in which they are known to occur, will be of value as indicating the present knowledge on the subject. It has seemed to me best to confine the list to the worms, and to exclude the protozoan parasites for the double reason that the latter are very imperfectly known, and it would be difficult to present a satisfactory list, and, in the second place, that they are also more difficult to determine, even by the professional microscopist, and present insuperable difficulties to the ordinary practitioner.

It may be confessed at the outset that the table is probably incomplete. The individual records are much scattered, and in such form as to demand extensive critical editing. It would be improbable, then, that, even with the great care which has been exercised, all records should have been included. So far as the list concerns Europe and the United States, however, I think it may be said that it is most nearly complete, and includes all but the most obscure records up to the present date. It should nevertheless be borne in mind that one may certainly expect further evidence of the presence of some of these species in unrecorded regions and of the existence of new species in most of the regions of the world. Additional strength is given to this general premise by the discoveries which have been made within the past decade in these United States. Thus Thayer has demonstrated the existence here of the Indo-European *Strongyloides stercoralis.* White has discovered the Asiatic *Opisthorchis sinensis,* I have found the Asiatic lung fluke, *Paragonimus Westermanii,* and a new human tapeworm, *Tænia confusa,* while Stiles, in addition to records on the vinegar eel, *Anguillula aceti,* and other forms new as human parasites here, has contributed the most important of all these studies, namely, that on the widespread occurrence of a new hook-worm, *Uncinaria americana,* which is of great etiologic significance over large areas of our country.[4]

---

[3] Ward, H. B.: Cestoda, Nematoda, Protozoa, Trematoda, Wood's Reference Handbook of Medical Sciences, Revised edition.

In the belief of the medical profession 200 years ago there was no disease, real or imaginary, which was not due to the presence and effect of some kind of parasite. Each ailment had its particular "worm" in its characteristic location. This was a direct result of the endeavor to reduce every malady to some definite cause, and from a joining of the unknown sickness with the parasites, of which they knew as little. Under the influence of study and of increase of knowledge regarding the parasites, such a theory was seen to be untenable, and the movement in the opposite direction began—a tendency which may be said by this time to have passed its height. In fact, there has prevailed during recent years among the medical men of this country an exaggerated idea of the unimportance of human parasites.

---

[4] Stiles, C. W.: The Significance of Recent Cases of Hookworm Disease, Eighteenth Annual Report, Bureau of Animal Industry

Parasite. (Scientific Name.)	Found as Human Parasite in		Type of Parasitism.	Recorded Frequency as Human Parasite.	Geographical Distribution.					
	Stage of Parasite.	Organ of Host.			Europe.	Asia.	Africa.	North America.	South America.	Australia.
Trematoda (flukes).										
Gastrodiscus hominis.	Adult	Colon.	Occasional	Twice.		†				
Fasciola hepatica.	"	Liver	"	Rare	†	§		§	§	§
Fasciola angusta.	"	?	?	Once.			§		‡?	
Fasciolopsis buski.	"	Intestine	Normal.	Rare		*				
Fasciolopsis rathouisi.	"	"	Occasional	Once.		†				
Paragonimus westermanii.	"	Lung	Normal.	Abundant.	§	*		§		
Opisthorchis felineus	"	Liver	"	Frequent	†	†		§		
Opisthorchis sinensis.	"	"	"	"		*		‡		
Opisthorchis noverca.	"	"	Occasional ?	Once.		†				
Metorchis truncatus	"	"	Occasional	" ?		†				
Heterophyes heterophyes	"	Intestine	Normal.	Frequent		§	*			
Dicrocoelium lanceatum	"	Liver	Occasional	Rare.	†	§	†	§	§	§
Schistosoma hæmatobium.	"	Portal vein.	Normal.	Frequent	‡	‡	*	‡		
Cestoda (tapeworms).										
Dibothriocephalus latus.	Adult	Intestine	Normal.	Abundant.	*	*	†	‡		
Dibothriocephalus cordatus.	"	"	Occasional	Rare	†			†		
Diplogonoporus grandis.	"	"	"	"		*				
Bothriocephalus mansoni	Larva.	Connective tissue.	"	"		†				
Dipylidium caninum	Adult	Intestine	"	"	†			†		
Hymenolepis nana	"	"	Normal ?.	Frequent.	†	†	†	†?	†	
Hymenolepis diminuta.	"	"	Occasional	Rare.	†			†	†	
Hymenolepis lanceolata	"	"	"	Once	†					
Davainea madagascariensis	"	"	"	Rare.		†	†		†	
Davainea(?) asiatica	"	"	?	Once.		†				
Tænia solium.	Adult.	"	Normal.	Abundant.	†	†	†	†		
Cysticercus cellulosæ	Larva.	Connective tissue	Occasional	Rare.	*			†		
Tænia saginata	Adult.	Intestine	Normal.	Abundant.	†	†	†	†		
Tænia marginata	Larva.	Connective tissue.	?	Once ?				†?		
Tænia serrata	Adult.	Intestine	Occasional	Twice ?			†?			
Tænia africana.	"	"	Normal ?	Once			†			
Tænia confusa	"	"	" ?	Twice				†		
Tænia echinococcus (Echinococcus polymorphus).	Larva.	Connective tissue.	Normal.	Frequent	*			†		†
Tænia hominis.	Adult.	Intestine	?	Once.		†				
Nematoda (round worms).										
Leptodera pellio.	Adult.	Vagina.	Accidental	Once.	†					
Leptodera niellyi.	Larva.	Skin	Accidental ?.	"	†					
Anguillula aceti	Adult	Bladder.	Accidental	Rare.				†		
Strongyloides stercoralis	"	Intestine	Normal.	Abundant.	†	*	*	†	†	
Gnathostoma siamense	"	Skin.	Occasional	Once.		†				
Filaria medinensis	"	"	Normal.	Abundant.	‡	*	*	†	†	
Filaria loa	"	Eye.	"	Frequent	‡		*	‡	‡	
Filaria volvulus	"	Lymph vessels	Normal ?	Rare.	‡	†?	*			
Filaria conjunctivæ	"	Conjunctiva.	Occasional	"	†					
Filaria lentis.	Young.	Eye.	?	Uncertain.	?	?				
Filaria restiformis	Adult.	Bladder ?.	?	Once.				†		
Filaria hominis oris	?	?	?	"				†		
Filaria labialis.	?	Lip	?	"	†					
Filaria lymphatica.	Adult.	Lymph vessels	Occasional ?	Twice.		†				
Filaria immitis.	?	?	?	Uncertain	†?	§		§	§	
Filaria bancrofti	Adult. Larva	Lymph vessels Blood.	Normal. "	Abundant Frequent	†?	*	*	†	†?	†
Filaria magalhaesi.	Adult. Larva.	Heart. Blood	Normal ?	Rare.					†	
Filaria perstans	Adult. Larva.	Connective tissue Blood.	" ?	Once	‡		*		†?	
Filaria diurna	Larva.	"	Normal.	Frequent			†			
Filaria demarquayi	"	"	Normal ?	Rare.				†		
Filaria romanorum-orientalis.	Adult	"	?	Once.	†					
Filaria ozzardi.	Adult ? Larva.	Connective tissue Blood.	Normal ?.	Rare.					†	
Filaria kilimaræ.	Adult.	Body cavity	?	Once.			†			
Trichuris trichiura	"	Colon.	Normal.	Abundant.	†	*	†	†		†
Trichinella spiralis.	Adult. Larva.	Intestine Muscle	" "	" "	†	†	†	†	†	†
Strongylus apri.	Adult	Lung.	Occasional	Rare.	†					
Strongylus subtilis.	"	Stomach	Normal ?	Twice.		†	†			
Dioctophyme renale	"	Kidney	Occasional	Rare.	†			§	§	
Uncinaria duodenalis	Adult. Larva.	Intestine Connective tissue	Normal. "	Abundant. "	†	†	†	†	†?	
Uncinaria americana.	Adult.	Intestine	"	"		†		*	†?	
Physaloptera caucasica	"	"	?	Once.		†				
Ascaris lumbricoides.	"	"	Normal.	Abundant.	†	†	†	†		
Ascaris canis	"	"	Occasional	Rare.	†			†		
Ascaris maritima.	" ?	?	?	Once.				†		
Oxyuris vermicularis.	"	Intestine	Normal.	Abundant.	†	†	†	†		
Gigantorhynchus gigas.	"	"	Occasional	Rare.	†?			§		
Gigantorhynchus moniliformis	"	"	"	"	†					
Echinorhynchus hominis.	"	"	?	Once.	†					

Explanation of signs,—* Recorded from man; autochthonous to region † Recorded from man; probably endemic, though often secondarily. ‡ Recorded from man; probably acquired elsewhere. § Recorded from some other host, hence possible in man. ? Record open to question.

It has been very generally maintained that the country was less infested than the old world, or that the forms, after all, were of little significance in the etiology of disease. I am of the opinion that the discoveries referred to furnish ample grounds for a modification of the position of indifference heretofore assumed, and in the treatment of disease call for more careful consideration of such forms as possible factors of etiologic significance. The clinical importance of parasites is generally recognized in such cases as bothriocephalus anemia, of which only a very few instances are on record in the United States, but similar significance has not been accorded to most forms.

Recent studies, however, have demonstrated the presence of hemoglobin in the alimentary canal of many nematode parasites, the pathologic effect of whose activities must be counted much more important than heretofore estimated by reason of this blood-sucking habit. Thus in cases of uncinariasis the amount of blood lost from myriads of minute hemorrhages imparts a characteristic reddish brown color to the feces, the intestinal wall becomes seriously affected, and affords places of easy attack for any pathogenic germs which may be present. This indirect damage may be very serious in the individual instance, and may include primarily or secondarily undesirable regressive or progressive histologic changes, inflammatory processes and disturbances in the circulation.

Another source of danger from parasites is one which has long been surmised, but only recently demonstrated. A number of investigators have shown that various *Cestoda, Acanthocephala* and *Eunematoda* contain definite poisons (toxins) which, when extracted and employed, experimentally, affect particularly the nervous system and the formation of blood. The continued formation and giving off of such a substance would explain the apparently excessive results of parasitism in some instances, results which are shown prominently in reflex nervous symptoms. In a certain proportion of cases, pernicious anemia is the result of this toxic effect, and is accompanied by a mortality of 17 per cent., according to one report regarding *Bothriocephalus*. Whether the poison is elaborated by the parasite, or is produced by pathologic processes in the worm, or by its death, as well as the ground for the variability in the toxic action of different specimens, are questions as yet undecided. It has been shown, however, that the extracts from different species of helminths vary considerably in toxic power. Vaullegeard has isolated two toxic principles, one of which acts on nerve centers and the other on muscles, and many symptoms, produced experimentally by the injection of these substances, are analogous to those manifested in parasitic disease. According to this chemical theory, the troubles caused by parasites are due to the formation of toxic substances more rapidly than their elimination of the host, and their consequent accumulation in the system. A striking instance of the actual effects of parasitism on a large scale is set forth by Stiles[4] in his description of the general anemic condition and the lowered physical and mental vitality of the families and communities where *Uncinaria americana* is common. These considerations are sufficient to show the greater numbers and more serious effects of human parasites in our own country than has been conceded hitherto.

In the next place it is necessary to emphasize the importance of the accurate identification of human parasites. They are by no means all of equal etiologic rank; some are known to exert deleterious effects on the human organism, regarding the action of some much doubt exists, and there are others which are believed to be indifferent to man. Furthermore, even of those whose injurious effects are unquestioned, the results on the hosts differ notably, and the line of successful treatment differs equally. It is evidently important, then, to determine accurately with what species the practitioner has to deal in the individual instance. To-day no one would be satisfied to accept the diagnosis of "fever," and how can the diagnosis of "worms" be regarded as more sufficient?

In reaching a precise determination, the physician has to deal usually with what is purely a microscopic question. The data which are essential are obtainable only by the use of the microscope, and yet they are very easily secured. They do not involve any complicated technic or the use of high powers, and a series of time-consuming cultures is entirely unnecessary. The determination is most readily made from fresh material, and, while it should be repeated several times in order to exclude all possibility of deception or accident, it requires only a brief time and the use of comparatively low magnification. A consideration of the factors involved will make the matter clearer.

Evidence of the presence of parasites will ordinarily be obtained by an examination of the blood, sputum, urine or feces. The first three are very frequently examined in the diagnosis of disease, and, as a matter of fact, they rarely furnish evidence of parasitism. So far as I have been able to learn, fecal examinations are rarely made, and yet by them evidence of parasitism would be most largely furnished.

By means of such examination one finds sometimes specimens of the entire adult parasite; again, recognizable fragments of the same, its embryos, or its eggs. It is comparatively rarely that one encounters specimens of the entire parasite, and unless the latter is very abundant, such specimens may easily be overlooked if not of such size as to be readily visible to the naked eye.

The identification of the parasite by some recognizable fragment of the body is regularly made only in the case of the tapeworm, which is determined by the passing of segments or proglottids at stools. While the precise determination of the species of tapeworm from the separate proglottids is often a matter of more difficulty than ordinarily believed, the cases of confusion resulting therefrom are not such as to introduce any difficulties in the accepted treatment. In passing, it may be noted, however, that the determination of tapeworm proglottids as flukes on account of their active independent movements is a frequent error. The examination of such structures, even with a hand lens, will show the absence of features characteristic of the flukes.

The determination of embryos is not attended with difficulties, so far as the different groups are concerned. The individual species of *Filaria* have been but little studied, and are imperfectly known. These forms are probably rare in our fauna, unless it be in the Southern states, and methods of coping with them are yet to be worked out.

It is ordinarily with the eggs of parasites, if found at all, that the greatest difficulties in precise determination are experienced. This is, in large part, due to the inaccurate and insufficient knowledge concerning them. A comparison of the original sources with various manuals shows that serious errors in measurement have crept in and that mention of important and characteristic peculiarities has often been omitted. I have, accordingly, published elsewhere[5] a critical review of these features, with illustrations to which those interested may be referred for details. Here it is possible to review only certain general features.

The eggs of parasites may be distinguished on the basis of form, size, texture and other individual peculiarities. Any one of these elements is usually insufficient for specific distinction; but, with the exception of a few forms of rare occurrence which are imperfectly known, the group of characters enables one to make a determination. In reaching a decision, the observer should, however, keep in mind certain general points. In the case of tapeworm eggs, there are sometimes ex-

---

5. Ward, H. B.: Data for the Determination of Human Parasites, Trans. Amer. Micros. Soc., vol. xxiv, 1903.

ternal membranes of a deciduous or variable character. Their presence in an extended or in a shrunken condition, or their absence, may alter greatly the external appearance of the eggs; the appearance and size of the inner membrane and of the included embryo are, however, relatively constant. The eggs of flukes and of round worms have only a single firm shell of chitinous character, and are in color usually a faint yellowish-brown, varying to darker brown. As the shell is firm, it can not be materially modified in size by pressure, although since the increase in width is relatively much greater, the proportions are noticeably altered. All eggs are not mathematically uniform in size; the range of variation is in most cases small, and the average readily obtained by measuring ten or a dozen specimens taken at random. The same comparison of a number of specimens will serve to eliminate abnormalities of the individual egg and to give a correct idea of the typical structure.

It is necessary now to call attention to possible results of the examination in the way of non-agreement of the forms discovered with the data at present known regarding human parasites. Such non-agreement may, of course, point to the discovery of a form new to the world, and most frequently has resulted in the description of the form under these conditions as a new species which has been duly baptized. Unfortunately, there are two other possibilities which are more frequently met with than the one just cited, and a disregard of them has led to great confusion. It may be, in the first place, that the species is new to the human host, but is one which is known from some other host. It, consequently, should not receive a new name, but should be discussed merely in the light of its occurrence under these conditions heretofore unknown. Such a species may be normal to the human host as well as to that from which it was previously known, but a considerable range of cases must be brought forward in order to demonstrate this fact. When only a single case of the occurrence of the parasite is determined, such new forms fall more frequently into the categories known as occasional parasites, and accidental parasites.

One may recognize among human parasites those which occur in their normal host, but in an unusual location, like the brain cysticerci; there are also many of the species listed which can not be regarded in any way as characteristic of the human host. Such are the occasional parasites which are species of true parasitic habit and able to attain normal development in the human host, but ordinarily not finding conditions favorable for their introduction. As an instance of such species may be mentioned *Fasciola hepatica,* the common liver fluke of the sheep, which in many regions of the world is extraordinarily abundant. That it can thrive in the human system is demonstrated by the score or more of definitely recorded cases of its occurrence there, but its infrequence is equal evidence of a general immunity on the part of man, lacking in these particular cases, or of some special feature in its life history which makes the infection of the human host difficult. That the latter is the probable explanation may be inferred from the fact that the cercaria larva, liberated from the intermediate host, encysts on plants and, hence, could only reach the human alimentary canal under unusual circumstances. Similar examples may be taken from other groups of parasitic forms, such as the rare occurrence in man of *Strongylus apri,* one of the commonest parasites of the pig in Europe, or of *Dipylidium caninum,* the cosmopolitan tapeworm of both dog and cat which has been reported only rarely from man.

Such occasional parasites often occur under abnormal conditions; thus, a fish nematode, *Ascaris clavata,* was discovered once in the hollow tooth of a man. Here the position was probably accidental, but in other cases it is the result of the action of the parasitc itself. So the red spiders, or "jigger" mites, of the central states bury themselves in the skin of man, although such a position is so clearly abnormal that, in fact, it destroys the chance of development and costs the parasite its life. A small leech, *Limnotis nilotica,* common in the circum-Mediterranean area, is often drawn into the throats of men and other animals drinking at wayside pools. It usually retains its position, causing serious difficulty, until removed by operative interference; hence it has become an occasional parasite of man rather than as most leeches, a temporary parasite; or one may regard it as falling in the next following group of accidental parasites. This example shows most clearly the narrow and somewhat artificial limits which separate these groups of parasites from one another. Of the mites also which have been reported a few times as obtained living from stomach, bladder and rectum, it is difficult to say whether they are occasional or accidental parasites of man.

There are also, rarely, other forms which usually occur free living, but which by chance are introduced into some organ in which conditions are such that they can thrive. They become thus accidental parasites, a group difficult practically to distinguish from the last, the occasional parasites, and yet presenting somewhat different biologic conditions. The recent discovery by Stiles and Frankland, as well as others, of the vinegar eel, *Anguillula aceti,* as an apparently successful colonizer of the bladder in a female patient, illustrates the type under consideration. There is little doubt that this parasite was introduced through the use of vinegar in vaginal douches and effected a successful colonization, possibly by virtue of the trace of albumin present in the urine which furnished the worms with nourishment. Equally striking is the case of Scheiber, who discovered *Pelodera pellio* in the urine of a female patient in Hungary. This typical slime-inhabiting nematode gained entrance no doubt through the application of mud poultices, which are commonly employed by peasants in that region. It should be noticed that such accidental parasites are necessarily confined to those groups of animals which have free living forms. Such are *Protozoa, Nematoda* and, perhaps, *Insecta* in the larval condition, while *Cestoda* and *Trematoda,* which live only as parasitic forms in some host, would become rather occasional parasites of man should they stray into the human system in some chance manner and find favorable conditions for existence.

Another type of animals found in man is quite distinct from those just considered. They are known as pseudoparasites and rank high in clinical importance. Among them one may recognize several very distinct classes. First, those which are actually free living animals, introduced by accident, usually in food or drink, into the human alimentary canal, and exciting there abnormal conditions which induce their more or less immediate and forcible expulsion. Thus Botkin found in the vomit of a Russian numbers of a small nematode which he wrongly believed to be a human parasite. In fact, it lives normally in the onion, and its introduction into the stomach with this food excited the untoward symptoms noted. Similarly, Blanchard records a case in which coleopterous larvæ were found in the vomit of a child.

That such may be the result of introducing a true parasite from some other host is indicated by several cases like that of *Ascaris maritima,* which Leuckart described from a single specimen vomited by a child in Greenland and which this author noted was very similar to *A. transfuga* of the brown bear. In all probability it was ingested with the viscera of some animal (seal?), though it may have been a species which had strayed into this unusual host only to make its appearance under the circumstances noted.

Of similar import are the cases of *Gordius,* the hair snake, which have been reported from man. In the adult condition this is normally a free living species, but about a dozen specimens have been taken from man after a supposed sojourn of from a few hours to fourteen days. Some of these have been vomited and others passed per anum. This form has often been passed off on the physician as a true parasite, and in one celebrated case at least as the Guinea worm.

In the same way one may find the explanation for other isolated cases of parasitism, even when the parasite is reported to have been passed from the alimentary canal. Thus Cobbold reported that larvæ of *Blaps mortisaga,* the English churchyard beetle, were found in fecal discharges, and many authors have recorded the presence of dipterous larvæ in the alimentary canal.

The majority of such observers has inclined to regard the larvæ as temporary endoparasites and to consider that they have accommodated themselves to the conditions present in the human host. Certain cases seem to show that these larvæ live for some time in the canal and often appear to evoke serious or even fatal disturbances; and yet the conclusions are open to grave doubt, for Calandruccio experimented extensively on two families, to which many of the supposed accidental parasites belong, and found that the ingested larvæ were regularly and promptly evacuated dead or dying, and in no case secured a footing in the canal.

Among the myriopods, about 40 recorded cases of pseudoparasitism have been brought together and discussed by Blanchard. In the large majority the animal was taken from the nasal fossæ, though in a smaller number it was actually obtained living from the alimentary canal, where it undoubtedly can exist for a brief time in spite of the untoward environment. The ingestion of such forms is purely accidental, the symptoms those of helminthiasis in general, and their stay at most very limited. They never show any evidence of adaptation to the new environment.

In some such accidental fashion other forms are sometimes introduced into various organs not connected with the alimentary system. Thus Trouessart reported the occurrence of a species of detricolous sarcoptids in the human testicle, where the mites formed an old colony in a painless cystic tumor.

In addition to the living animals of the types noted, the second class of pseudoparasites includes a large number of other structures which have been described as parasites. These may be considered conveniently in a few groups, the first of which includes bodies which are parts of the so-called host animal itself. Thus fragments of the arteria hyaloidea have been described as eye worms (*Filaria lentis, F. oculi-humani,* etc.); the supposed organisms of whooping cough are nothing more nor less than ciliated tracheal cells torn from the wall and found in the sputum in distorted form, while groups of small axillary and inguinal glands, hydatid moles and pacchionian bodies from the arachnoid have been frequently put on record as hydatid cysts.

Parts of substances used as food, both of plant and of animal origin, which have not been destroyed by the action of digestive juices, are also among the pseudoparasites of man. The radulæ of the common limpet have been reported several times from stools; the seeds of the mulberry were duly baptized as parasitic worms; and plant vessels and other similar undigested structures of peculiar appearance appear periodically as new helminths. That a differentiation of such structures is not simple appears from the account given by Stiles of the partially digested banana fibers, which closely simulate minute tapeworms. Some years ago Leuckart entrapped a group of research students in helminthology with the pulp vesicles of an orange which were found in a fecal examination.

In all of the cases considered above, it has been presupposed that the structures obtained actually came from within the human body. It is necessary, however, that the physician should have personal evidence of this, for there is another class of objects of which it can not be said. And these structures deserve brief mention in closing.

In determining the nature of unusual forms reported from man, it should always be kept in mind that in the absence of positive personal evidence, suspicion in cases of neurasthenia at least favors the deceitful introduction of such doubtful bodies. In many cases on record such things as earthworms, chicken entrails, etc., have been forcibly introduced into the rectum or vagina and have been subsequently reported by the attending physician as undoubted human entozoa of a remarkable character! Here, as elsewhere, the appearance of unusual structures should at once arouse the suspicion of the physician and call forth a most searching examination of the case in all its factors that any deceit be disclosed, or that in the event of the discovery of some rare parasite all conditions connected with its appearance be put on record for future use. Furthermore, it is important to preserve the fullest data in regard to any substances associated with it, as well as the food of the patient, whether usual or unusual, since in this way some hint as to the introduction of the supposed parasite may be found.

Finally, it is important to direct attention to the wisdom of preserving all doubtful material, whether new or not, in considerable quantities, and both the eggs and embryos, as well as the adults, or as many thereof as can be obtained. In case of doubt regarding the identification of species, or possible question as to the source, it is important that the material or some portion of it should be referred to some expert helminthologist for examination and verification of the result attained. It is always a pleasure to have the opportunity of examining such material, and to assist one's colleagues in any way in connection with such studies. In most cases, in fact, and especially such as deal with the occurrence of rare forms, or such as are new, it is desirable that such corroborative evidence should be secured before publication, for in this way is often prevented the confusion which arises from incorrect descriptions or from the publication of new names which are merely synonymous with those already known to science. As a matter of fact, the practitioner can hardly hope to be acquainted with the entire range of parasitic species, and if to the accurate observations which he records regarding the clinical side of the question can be appended the notes of some helminthologist who is in a position to give an expert opinion regarding the other side, the results are far more valuable to the world from their rounded scientific character and permanent value, than could be attained by the publication of either group of factors separately.

The large number of parasites in other animals which some unusual combination of circumstances may bring into the human system makes it imperative that any supposedly new species be submitted to the judgment of a specialist before it is described as such. Only in this way can the discoverer avoid adding to the long list of synonyms which already burden the literature of this subject and render it so difficult for the investigator not a specialist in this particular line to find his way aright.

DISCUSSION.

Dr. Frank B. Wynn, Indianapolis—First, I want to refer to a clinical case in the practice of W. B. Fletcher of Indianapolis. A patient had suffered for a long period from seizures of an epileptic nature of severe type. Segments of tapeworms were found in the stools. After the administration of proper remedies the parasite was expelled and the patient had complete relief from all symptoms.

A word in reference to spurious helminths. I recently had sent to me by a physician worms alleged to have been passed in the stools of a woman. They were the larvæ of the bluebottle fly. As she was said to be passing these in large numbers, I asked for a second sample and found them different from the first. A third supply revealed still a different species. So my first suspicions were confirmed, that a hysterical patient was practicing deception on the Doctor.

Dr. Ward has referred to one feature of great practical importance, which I should like to emphasize if possible, and that is the errors of practitioners in dealing with supposed intestinal parasites. Some two years ago I received from a doctor some little dark threads, passed in the stools of a patient and thought to be worms. Since then I have received two other specimens, identically similar from different patients. Under the microscope were to be seen chains of large, amber-colored oval bodies. My first impression was that they were uric acid nuggets formed on a cotton fibril in the vessel where the excreta had been passed, and that the sharp points of the crystals had been dissolved off as the urine became alkaline. By and by I found spirals, proving the vegetable character of the bodies. The next point of interest to determine was from what vegetable they came. In conjunction with my botanical friend, John S. Wright, it was soon demonstrated that these dark strings were of the fibrovascular tissue of the banana, especially the older fruit near the core. Age or light leads to pigmentation of the rows of large parenchyma cells along the strings of fibrovascular tissue. (The specimens exhibited were reported to the Indianapolis Medical Society about two years ago.)

Shortly after this investigation I received another specimen supposed to be tapeworm. The segments were too long and slender, however, and instead of being square cut were oblique at the ends. I suspected they were vegetable in character, and on investigation they were proven to be cabbage, prepared as slaw. (Specimen exhibited.)

I want to call attention to another structure not rarely found in the stools which I had some difficulty in running down. Dr. Ward informs me that he had a similar experience. I refer to the fusiform and attenuated masses of cells found in the lemon and orange, which are not unlike the fluke. Some were sent to me two years ago, supposed to be parasites.

These experiences led me to start some of my students in the medical department of the University of Indianapolis to studying some of the more common fruits and vegetables used as articles of diet. The results are presented in the Scientific Exhibit. First, sections were prepared of crude vegetable or fruit. Secondly, fresh glycerin mounts were made of the same articles, as found on the table ready for eating. And thirdly, each student ate abundantly of the article assigned, and afterward his stools were carefully examined for remnants of the food taken. We found that a number of these examinations showed products which might easily be mistaken for parasites. The fibrovascular threads of the pineapple, rhubarb and celery are particularly apt to mislead, as will be readily appreciated from the specimens here exhibited.

The specimen I have here came from my own stools. I was surprised to find these long flakes, not unlike tapeworms. It proves to be paper. Paper intimately adherent to candy, meat from the butcher shop, bread, etc., is often swallowed unconsciously, is wholly indigestible and might be mistaken for the segments of tapeworm or membranous exfoliation of colitis.

Dr. Walter L. Bierring, Iowa City, Iowa—In connection with the remarks made by Dr. Wynn, I would like to refer to an experience with the spurious tapeworm disease in Iowa during the past winter. Two specimens of material were sent to me from different parts of the state, in both cases being derived from the stools of children 5 years of age. Periodical attacks of indigestion were noted and when this tapeworm-like material was passed the child in each instance improved. One of the specimens came from one of the best physicians of our state, who entertained an idea that it might be a case of *Tœnia nana* infection. After repeated examination of the material and suspecting it to be some vegetable fiber, I referred it to Dr. Stiles of Washington, who informed me that the tapeworm-like material was composed of undigested banana fibers. For the purpose of corroboration various tests were made in the pathologic laboratory, one of which consisted in giving test meals of banana and finding the dark-colored segmented fibers subsequently in the stool, and the other consisted in applying a 10 per cent. solution of potassium hydrate to banana, which brought the transverse fibers of the banana that are evidently indigestible out very prominently, also giving to them the dark color which they usually attain on exposure to the light.

Dr. Allen J. Smith, Galveston, Texas—I have found that almost every living thing is possessed of some parasite, and they have a widespread pathogenic influence. The subject is one obtaining greater recognition within recent years, as shown by the increasing prominence given it in pathologic text-books; but as yet in this country it has by no means had sufficient stress laid on it. There is not as yet sufficient demand for information on the lines of the paper just read to have called forth a single good text-book in our language. There are a number of excellent German and French works dealing in an authoritative and systematic manner with human and comparative zoöparasitology, but none in our own tongue (except the work written by Neumann for veterinarians and translated from the German). Within the past three years I have approached no less than six of the more prominent American medical book publishers with a proposition to publish a translation of Railliet's *Traite de Zoologie médicale et agricole,* but all declined on the ground of financial danger. I regret my failure, as the work in hand of many practitioners in this country really presents a great need for some standard work of the kind. As an illustration of the importance of the general subject, I call attention to the recent work of a number of observers in relation to the new American hookworm, *Uncinaria americana* (Stiles); a parasite first discovered in Galveston, and since then met by a number of observers in the southern and eastern parts of the country. The excellent work of Stiles, of the United States Public Health and Marine-Hospital Service, has demonstrated how this parasite is probably wholly or at least largely responsible for the miserable state of the well-known "poor whites," known so widely as dirt "eaters" in these districts, pale, large-bellied and thin, for the inertness and laziness for which they are so much criticised, as well as for really serious pathologic conditions in these people. Aside from its proper influences this parasite seems to seriously influence and perhaps modify the course of other diseases with which it may be associated; for example, it probably is an influence making malaria more persistent. From observations of my own, where the uncinaria and malarial parasites coexisted, I have noted the difficulty in getting rid of the malarial infection by the usual use of quinin until the intestinal parasites have been disposed of—a relationship perhaps depending on the influence of the latter in keeping at a low ebb the natural antagonistic powers of the body against the malarial organisms and thus permitting redevelopment of any hematozoa remaining after a course of quinin administration. This I have so persistently noted that I feel the importance of seeking the coexistence of these intestinal parasites in the particularly obstinate, chronic and recurrent forms of malaria in these southern districts as possible influences in the clinical course of such a case.

Another example of the importance of the subject is the recent discovery in Texas and elsewhere of *Tœnia nana*, a tapeworm known to be responsible for considerable intestinal disturbance, for the development of pernicious anemia and in various instances of epileptiform phenomena. Such instances of the importance of animal parasites might be indefinitely multiplied; and the importance of this branch of pathology is manifesting itself more and more as time goes on. The field, however, has by no means received the attention its importance deserves; and for one I feel anxious that it shall soon be represented by some adequate reference work in our own language, or some translation of one of the worthy European works annotated from an American standpoint.

Dr. H. B. Ward, Lincoln, Neb.—I think Dr. Wynn's date of two years is the record for the banana fibers, though within that time Stiles of Washington, Bierring of Iowa and a number of men in different parts of the country have made the same discovery. One case to which I did not refer in the paper came to me last year in Nebraska, which has the further interest that the physician said it was a remarkable case of tapeworm, as it was found in the alimentary canal and also in the vagina.

One thing I should like to emphasize in closing. It has been mentioned again and again to-day in this and in other sections that there is a sad lack of fecal examinations. Last year a very well educated and a very bright and thoughtful physician in a city not my own permitted a patient to die of pernicious anemia without a single fecal examination.

CONDITION OF THE ENDOMETRIUM IN CASES OF UTERINE MYOMATA.

THOMAS S. CULLEN, M.B.
BALTIMORE.

CERVIX.

As a rule the cervical mucosa shows no change. Occasionally, however, cervical polypi are present or the cervical glands may be moderately or markedly dilated. In rare instances true cervical erosion, in other words an ulceration of the cervix, exists, and now and then squamous-cell carcinoma or adenocarcinoma of the cervix may be associated with myomata. Where the cervix is much lengthened out the glands are often unraveled. We then note the squamous epithelium of the cervix alternating with that of the unfolded glands.

BODY.

Endometritis is occasionally found; when present it is almost invariably associated with inflammatory changes in the adnexa.

Tuberculosis is not uncommon, but while sometimes occurring independently, is usually associated with similar processes in the fallopian tubes.

Finger-like or dome-like projections from the mucosa have been seen from time to time, and also other pictures more or less suggestive of a malignant change.

Adenocarcinoma of the body of the uterus is quite frequently associated with myomata, as we have noted elsewhere. In the majority of cases it was not suspected.

While any of the foregoing conditions may exist, yet in nearly all instances the changes present are entirely mechanical. If myomata are subperitoneal or intraligamentary, the mucosa is usually normal, provided the tubes are unaltered. When a nodule impinges on the cavity the mucosa over the most prominent part becomes stretched and thinned out. This progresses until eventually there is nothing but the surface epithelium covering the nodule. While this atrophy is increasing the mucosa in the depressions at the sides remains unaltered or becomes thicker. This thickening is occasionally due to simple gland hypertrophy. Portions of the mucosa are often mechanically forced out into the cavity, producing polypi. With the distortion of the mucosa the glands sometimes become blocked, producing small cystic dilatations. The glands of the mucosa are sometimes much dilated, and not infrequently there is considerable edema. When the myoma becomes entirely submucous it is usually covered by a thin layer of mucosa, but in a few instances we have seen a sloughing cavity in the myoma opening directly into the uterine cavity. Now and then a submucous myoma from the posterior wall will blend with the similar nodule in the anterior wall, obliterating the mucosa entirely over a given area.

From an examination of a great many specimens we can lay down the general rule that where the fallopian tubes are normal and where no sloughing submucous myoma is present, that the uterine mucosa will be perfectly normal or show simple mechanical changes. The import to the surgeon is that where such favorable conditions are present he can do a myomectomy, opening, if necessary, a large part of the uterine cavity with little danger of infection. On the other hand, if the tubes be adherent, or a sloughing submucous myoma be present, complete removal of the uterus is indicated, the sloughing submucous nodule, of course, being removed some time prior to performing the hysterectomy.

These results are based on the gross or histologic examination of nearly one thousand cases.

A CASE OF AEROGENES CAPSULATUS INFECTION OF THE NECK.

LOUIS LEROY, B.S., M.D.
Professor of Pathology and Bacteriology, Vanderbilt University.
NASHVILLE, TENN.

The case which I have to report is one of some interest from the rather infrequent occurrence and from the fact that the *Bacillus aerogenes capsulatus* was obtained from the wound six days before death.

W. F.—Age 23, black, male, single, laborer, muscular and vigorous; family history negative. Entered hospital January 27, died Feb. 4, 1903.

Gave history of having had a "sore throat," with considerable swelling of left side of the neck in the region of the tonsil. The symptoms referable to the throat lessened,. but the external conditions became worse, developing considerable swelling and pain.

His physician, seeing him for the first time at night, made the diagnosis of erysipelas. Later the diagnosis at the hospital was made of suppurative cellulitis of face and neck. At this time his pulse was 128, respiration 30, temperature 102.

An incision was made, from which a small amount of dark fluid exuded, but no pus. Thorough irrigation every four hours with bichlorid of mercury was instituted without visible result. The inflammatory reaction around the wound was not at all severe, and after the second day the skin below the incision slowly separated from the subcutaneous tissue, until at the fourth day a gangrenous area was present reaching from the ear to the clavicle, and discharging a light sanguineous fluid from an opening at the lower edge. About the fifth day the skin was entirely separated, leaving the muscles beneath clearly exposed. The fibrous tissue rapidly became destroyed, leaving the underlying muscles, vesicles and nerves clearly exposed to view as in the most careful dissection.

The swelling was not extreme, and until the last day no emphysema or crepitation was present, and then only in small amount.

The temperature ranged from 102 to 105, being with difficulty kept below 104 by ice caps and baths.

The pulse varied from 128 on admission to 140 at the time of death. Until within a few hours of his death it was full and strong, despite its rapidity.

The respirations were rapid, varying from 28 to 34 most of the time, although there were times when it dropped as low as 20 to the minute.

The urine showed a progressive diminution in quantity, specific gravity, total solids, percentage and total elimination of urea, chlorid, phosphates and sulphates.

The reaction was acid throughout. Traces of albumin and bile were present for the first two days, but did not appear again.

The microscopic examination was negative in all the daily examinations.

The blood examinations were of some interest, showing a progressive decrease in the number of erythrocytes, percentage of hemoglobin, specific gravity and hemoglobin index.

The leucocytes showed a progressively increasing infectious leucocytosis until twelve hours before death, when an enormous drop in their number apparently heralded the end of the patient's ability to react. Up to this time he had been cheerful, declaring that he would be entirely well in a few days.

The decrease in leucocytes was mostly due to a great diminution in the number of neutrophiles, which fell from 86 per cent. to 40 per cent.—almost even with the small lymphocytes, which in turn showed a reciprocal increase.

The full results of the blood examinations may be seen at a glance from the accompanying table.

No bacilli were observed in smears of the blood during these examinations. The last day, about 12 hours before death, some irregularity in the red cells appeared, a number of poikilocytes and microcytes being observed, but at no time were any nucleated red cells noted.

An examination of the pus was made six days before death. In smears a large number of bacteria were observed, but streptococci seemed to be absent. Other cocci staining by Gram's method were present, and a few large bacilli, which in all probability were *Bacillus aerogenes capsulatus,* but on which I was unable to demonstrate any capsule, either in ordinarily prepared specimens or by the special methods of capsule demonstration. Some of the pus was collected in sterile capillary tubes, and from these aërobic and anaërobic cultures were made within 15 minutes of its collection. The aërobic cultures were made in ordinary agar in Petri dishes in the incubator. The anaërobic cultures were made by the method of Veillon. In this method a number (15 to 20) of large test tubes of glucose agar are melted by immersion in boiling water for an hour in order to expel all the air. They are then allowed to cool to within a degree or two of the point of solidification, when one of the infected capillary tubes is plunged to the bottom of the agar and its contents expelled by blowing. As soon as the agar is inoculated it is solidified at once by plunging it into ice water. The capillary tube is then immersed into each of the series of agar tubes blowing gently into it and agitating it at the same time. In this way a number of the tubes will be inoculated, the number of colonies varying from one or two in each tube to a number too great to count. All the tubes are now placed in the incubator until the colonies develop sufficiently to be studied. Cultures obtained in this way developed a large number of colonies in the deeper layers of the tubes, which were subsequently separated into a strict anaërobe and four aërobic organisms. The strict anaërobe was determined to be the *Bacillus aerogenes capsulatus* of Welch, although in the beginning some uncertainty arose from the absence of a capsule and lack of gas generation in the wound. Both of these characteristics were, however, observed in subsequent inoculation experiments. The following biologic characteristics were determined and verified in the work of investigation.

The organism is a strict anaërobe, but will grow in deep layers of glucose agar in Veillon's method. I was unable to obtain more than a trace of growth by deep stick culture.

In hydrogen, illuminating gas, carbon dioxid and by the pyrogallic acid method growth will result, but best in an atmosphere of hydrogen. Good growths were also obtained under a layer of *Bacillus subtilis.*

RECORD OF BLOOD EXAMINATIONS.

Date, 1903.	Jan. 28.	Feb. 1.	Feb. 2.	Feb. 4.
Red blood cells	4,802,000	4,265,000	3,840,000	3,121,000
Leucocytes	19,524	36,742	72,800	11,121
Specific gravity	1052.5	1046	1037	1030
	Per cent.	Per cent.	Per cent.	Per cent.
Hemoglobin, specific gravity	72	52	33	20
Hemoglobin (Gowers')	70	49	38	28
Hemoglobin index	74	57	49	32
Small lymphocytes	6.2	7.6	......	37.3
Large lymphocytes	3.8	5.1	......	22.2
Neutrophiles	89.7	86.3	......	40.1
Eosinophiles	0.3	1	......	1.4
Poikilocytes	......	......	......	few
Microcytes	......	......	......	few

* Twelve hours before death.

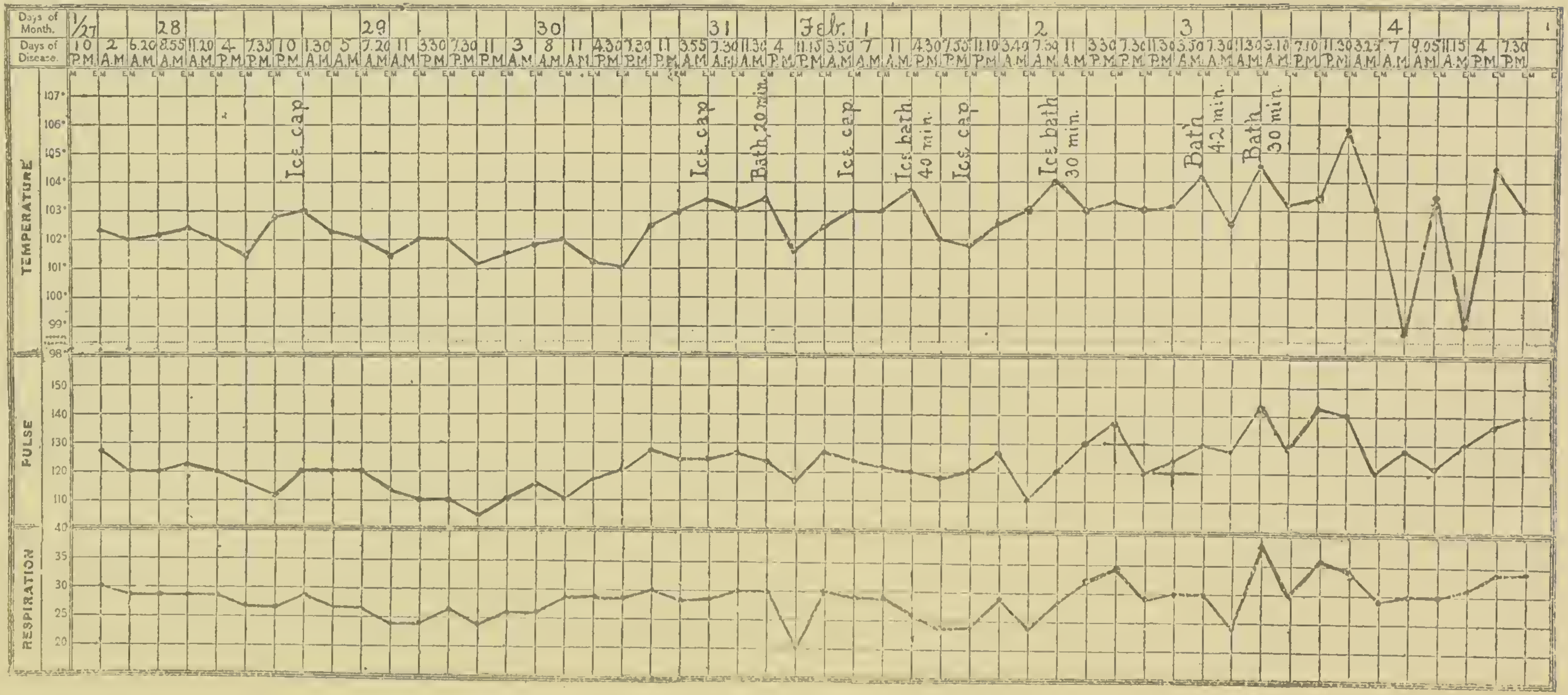
RECORD OF URINARY EXAMINATIONS.

Date,1903	Jan. 28.	Jan. 9.	Jan. 30.	Jan. 31.	Feb. .	Feb. 2.	Feb. 3.	Feb. 4.
Transparency..	Hazy...	Hazy...	Hazy...	Hazy...	Hazy...	Hazy...	Hazy...	Hazy...
Color . .	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Specific gravity	1018	1018	1018	1016	1014	1010	1010	1008
React'on	Acid . .	Acid. .	Acid. .	Acid. .	Acid. .	Acid. .	Acid. .	Acid. .
Quantity (24 hr.)	1350		*		*	1299	*	1200
Total solids.	56.61	*	*	*	*	30.29		23.32
Urea...	1.952	1.9	1.8	1.75	1.6	1.2	1.4	1.2
Total urea (24 hr.)	26.32	*	*			15.48	*	12.0
Chlorids	6%	*	*				*	3%
Phosphates	1%	.8%	.6%	.5%	.4%	0.5%	.3%	0.25
Sulphates	2%	*	*	*	*	0.75	*	0.5
Sugar . .	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Mucin. .	Abund.	Abund.	Abund.	Abund.	Abund,	Abund.	Abund.	Abund.
Albumin	Trace..	Trace..	Absent	Absent	Absent	Absent	Absent	Absent
Bile... .	"	"	"	"	"	"	"	"
Microscopic.	Neg..	Neg.. .	Neg.. .	Neg.. .	Neg.. .	Neg.. .	Neg.. .	Neg.. .

* Not recorded.

The bacillus grows slowly at the room temperature on all media if the oxygen conditions are favorable. They resisted a temperature between 5 and 0 C. for twenty-four hours. The thermal death point was not determined.

When developed in plate cultures in an atmosphere of hydrogen the colonies may reach a size of 1 mm. in diameter in forty-eight hours in the incubator. These colonies are round, convex and smooth. They refract the light strongly and are finely granular when examined under a low magnification. The edges of the colonies are entire. By reflected light the colonies are whitish opalescent. By transmitted light they are a smoky brown. The bacilli are about the size of anthrax, but the ends are usually rounded. They are frequently found singly, usually in pairs or threes, and once a chain of twenty elements was found. In bouillon cultures they appeared to be somewhat shorter than on solid media. They stain easily, but irregularly, by all the common dyes and also by Gram's method. Old colonies show many individuals who do not take Gram's stain, and chains were observed in which alternate cells only remained stained by Gram's method, the intermediate ones being decolorized. The water of condensation, or rather the small amount of water squeezed out of the agar on cooling, contained the most luxuriant growth, despite the fact that it was exposed to the air. This is accounted for, as pointed out by Novy in the case of *Bacillus oedematis maligni II,* by the fact that the oxygen in the water has been displaced by other gases produced by the bacilli deeper in the tube. It might also be noticed that much of the air was previously expelled from this water during the melting of the agar and that the conditions are not favorable for absorption of much oxygen. In all sugar-containing media large amounts of gas were generated, the bubbles beginning to show in six hours, and in twenty-four hours in most cases the agar would be broken in several places and pushed up against the cotton plug. Some gas was produced in media containing no sugar, but in small amount. Gelatin was very slowly liquefied. One series of tubes kept in the incubator in hydrogen for three weeks refused to solidify on being again cooled, while the controls solidified readily.


Days of Month.
Days of Disease.
1/27
28
29
30
31
Febr. 1
2
3
4
TEMPERATURE
PULSE
RESPIRATION
107°
106°
105°
104°
103°
102°
101°
100°
99°
98
150
140
130
120
110
40
35
30
25
20
Ice cap
Ice cap
Bath, 20 min.
Ice cap
Ice bath 40 min.
Ice cap
Ice bath 30 min.
Bath 42 min.
Bath 30 min.

The organism appeared to be non-motile, and no flagellæ or giant whips were found.

Spores were found once on an old Loeffler's blood serum culture which had been in the incubator in a Novy jar of hydrogen for seven days, and again on a plain agar reimplantation from the blood serum tube. The spores were central and did not cause any increase in the transverse diameter of the cell. All culture media became intensely acid within twelve hours of growth. This was also the case with the tissues of animals which died from inoculation, and in one test made from the secretion from the lesion of the patient. In this case the secretion had collected to the amount of about 1 c.c. in a necrotic pocket between the skin and underlying tissue. This was so intensely acid that I call attention to it as of possible subsequent value as an early diagnostic point. Litmus milk was precipitated and decolorized without being rendered, and a clear fluid left above the coagulum.

In pure culture in intravenous injection about half of the rabbits inoculated died and the bacillus was recovered from the heart's blood and tissues. Dogs were more refractory. When mixed cultures of *Staphylococcus aureus* and *Bacillus aerogenes capsulatus* were given subcutaneously large sloughing areas of necrosis followed in four out of five cases. The last case formed an abscess cavity which discharged pus containing both bacteria through a small fistulous opening, and finally healed completely.

In another series of inoculations in dogs, through cleansing of the necrotic area with hydrogen peroxid, it resulted in recovery.

A rabbit in which 1 c.c. of a bouillon culture had been injected in the ear was killed, as suggested by Welch of Baltimore, and in twenty-four hours the characteristic swelling occurred. This was allowed to progress at the room temperature for four days, when the distension was enormous. The gas was then collected over water through a canula and found to contain CO_2 hydrogen and a trace of H_2S.

It burned with a very white, bright flame, resembling, although not so intense, the flame of acetylene gas. I believe that this is the first case reported in which the infection in all probability entered the tissue through the throat and without history of an abrasion or lesion of the epithelium.

DISCUSSION.

Dr. L. Hektoen, Chicago—In connection with this interesting case I would refer to one in which the infection took place through a transfusion puncture of the skin in the submammary region. Spreading emphysema appeared and after death a general infection of the *Bacillus aerogenes capsulatus* was demonstrated.

Dr. Louis Leroy, Nashville, Tenn.—The bichlorid treatment was carried on in this case for a number of days without effect. In the experiments with animals peroxid of hydrogen seemed to stop the process almost within a day. I believe that further observations on the reaction of the pus in such infections will prove of value.

NEUROGLIA TISSUE AND EPENDYMAL EPITHELIUM IN TERATOID TUMORS.

HENRY A. CHRISTIAN, A.M., M.D.
Instructor in Pathology, Harvard University; Second Assistant Visiting Pathologist, the Boston City Hospital, and Assistant Pathologist, the Children's Hospital.
BOSTON.

(From the Sears Pathological Laboratory of Harvard University, and the Pathological Laboratory of the Boston City Hospital.)

In pathology the advances by which our knowledge of any subject is obtained often take the form of a wave. An epidemic occasions renewed interest and furnishes abundant fresh material; a new technical procedure stimulates investigation and invites the reëxamination of accumulated material: the result is a series of contributions revealing new facts concerning the subject. Such a period of activity was inaugurated in the study of neuroglia tissue by the publication in 1895 of the staining methods of Weigert[1] and of Mallory.[2] Since then has come most of our knowledge of this tissue. Many investigators have been engaged on its problems, and other staining methods have been introduced, but none of these differential methods appears to have been applied to any extent in the examination of similar elements in teratoid tumors. In a teratoma of the ovary, some features of which have already been published,[3] a large amount of neuroglia tissue was found. This finding occasioned the investigation of other tumors of this class with particular reference to neuroglia elements. As in these tumors structures related to neuroglia occur and by the application of various neuroglia staining methods other elements than neuroglia fibers are brought out, it has seemed well to consider all of these in this study. Hence neuroglia fibers, neuroglia cells, ependyma, dots and fibers which stain by the neuroglia staining methods and retina-like structures will here be described and their significance discussed.

---

[1] Weigert: Beiträge zur Kenntniss der normalen menschlichen Neuroglia, Frankfurt a. M., 1895.

[2] Mallory: Ueber gewisse Färbereactionen der Neuroglia, Centralbl. f. allgemein. Path., 1895, vi, 753.

[3] Christian: Ependymal Epithelium as a Constituent of a Teratoma, Medical Reports of the Boston City Hospital, 1902, xiii, 161; Boston Med. and Surg. Journal, 1902, cxlvii, 673.

Teratoid tumors have from earliest times received much attention. A great variety of forms has been described and all kinds of tissue, including the elements of the central nervous system, have been found in them. Their rate of growth and the symptoms due to their presence in various regions have been investigated. The contributions made to the various aspects of the subject have been reviewed repeatedly and it is not necessary to do so again at this time when it is our intention to consider mainly the histology of the neuroglia and of the ependymal epithelium in some of these tumors.

There were available for this study twenty teratoid tumors preserved in a way suitable for the application of neuroglia staining methods. Of these, 18 were from the ovary, one from the lung, and one from the anterior mediastinum. The tumors vary much in size and shape. Some consist of a single cyst with a solid ingrowth; some are solid cystic structures; others a combination of the two. All contain islands of bone and cartilage, some teeth. In six neuroglia was found. Of these, tumors 1, 2, 4, 5 and 6 arose in the ovary, tumor 3 in the lung. However, the possible presence of neuroglia in the others can not be denied, as it is manifestly impossible to exclude small areas of neuroglia except by serial examination of the tumor and this for such large tumors would be excessively laborious. For this reason and owing to the comparatively small number examined, these observations have no statistical value as to the frequency of the presence of neuroglia elements in teratoid tumors. They do show, however, that this tissue is of quite frequent occurrence in tumors not specially selected for complexity of structure.

Material from all of these tumors was fixed and preserved in 10 per cent. of formaldehyd. From some material was fixed in Zenker's fluid and preserved in 80 per cent. alcohol. Material fixed in formaldehyd was stained by Mallory's phosphotungstic acid hematoxylin method,[4] Mallory's modified fibrin method,[5] and Huber's modification of Benda's method of staining neuroglia.[6] That fixed in Zenker's fluid was stained by Mallory's anilin blue connective tissue stain[4] and the acid fuchsin potassium permanganate method very recently introduced by Mallory.[7] A number of variations and modifications of these methods were also employed and gave some interesting pictures. Besides these, alum hematein and eosin, or eosin and Unna's alkaline methylene blue were used. As many of these methods as possible were utilized in the study of each tumor.*

Neuroglia tissue is most abundant in tumor 1. The tumor consists of a single large cyst, with epidermal lining and an equal amount of tissue containing innumerable cysts, varying in size from very minute ones to those measuring several cm. in diameter. Between the cysts the neuroglia is scattered in masses of varying size and shape. None of these exceeds 1 cm. in greatest diameter. Most are very much smaller. Many of the areas are sharply circumscribed from the surrounding connective tissue. Into others strands of connective tissue penetrate or, on the other hand, a band of neuroglia makes its way for some distance from an otherwise sharply contoured mass into the surrounding connective tissue. Less often there is so intimate an intermingling along the border of the two tissues that the limits of the neuroglia can with the greatest difficulty be made out. In some sections single fibers or groups of several parallel fibers which resemble neuroglia fibers are found in the midst of connective tissue. These fibers are either fine or coarse, and have the same general direction as the surrounding connective tissue fibers. They

---

[4] Mallory: A Contribution to Staining Methods. Jour. of Exp. Med., 1900, v, 15.

[5] Mallory and Wright: Pathological Technique. Philadelphia, 1901, 328.

[6] Huber: Studies on the Neuroglia, Am. Jour. of Anat., 1901, I, 45.

[7] Mallory: A Hitherto Undescribed Fibrillar Substance Produced by Connective Tissue Cells, read at a meeting of the Am. Assoc. of Pathologists and Bacteriologists, Washington, D. C., May 14, 1903; to appear in Journal of Medical Research.

* Weigert's method of staining neuroglia was tried, but satisfactory results could not be obtained. This may have been due to the fact that the tumors were not hardened soon enough after removal from the body or that the reagents used by me differed in some way from those originally employed by Weigert. On this account deductions made by me in regard to neuroglia staining methods are not to be taken as applying to the Weigert method.

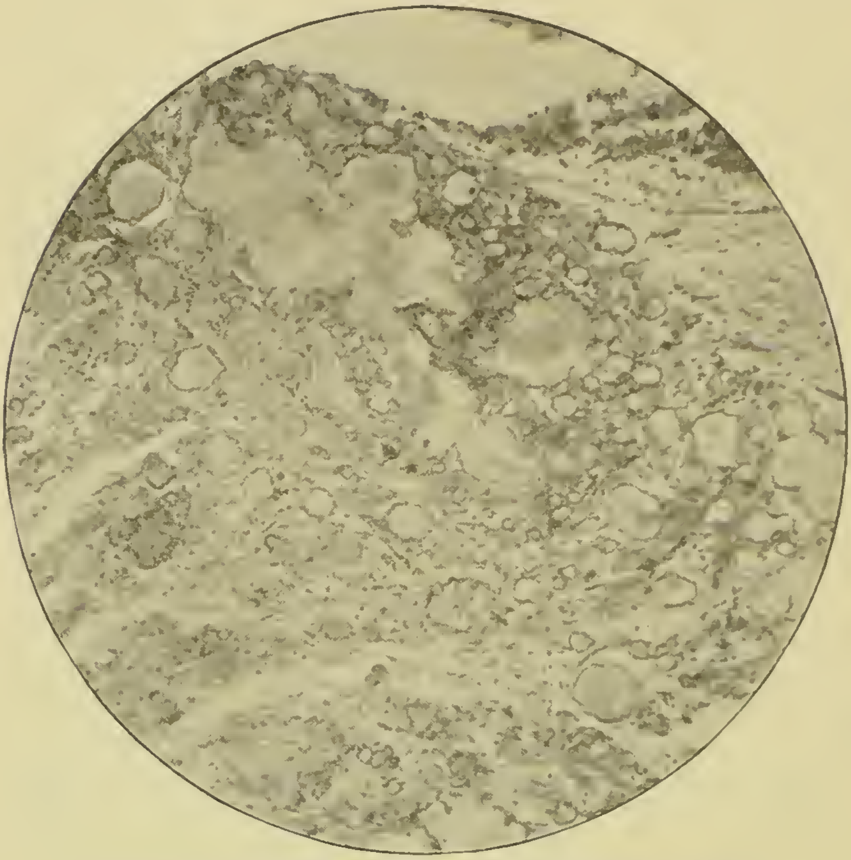


Fig. 1.—Corpora amylacea in neuroglia tissue.

may bear no relation of continuity to any mass of neuroglia tissue, and may be unaccompanied by any cell differing in appearance from the ordinary type of connective tissue cell.

The relation of the neuroglia to the cysts varies. Many neuroglia masses are entirely separated by connective tissue from the cysts. Others abut on or project into cysts. Some cysts are completely surrounded by neuroglia. There may be a large cyst with a comparatively thin layer of neuroglia about it or cysts of varying size may lie in the midst of large masses of neuroglia. Where the neuroglia is adjacent to a cyst it may be naked or covered by epithelium. The epithelium covering the neuroglia is of two general types. The one is flat cuboidal and lies immediately on neuroglia fibers, though none penetrates between them; the other is of high cylindrical type, and between these

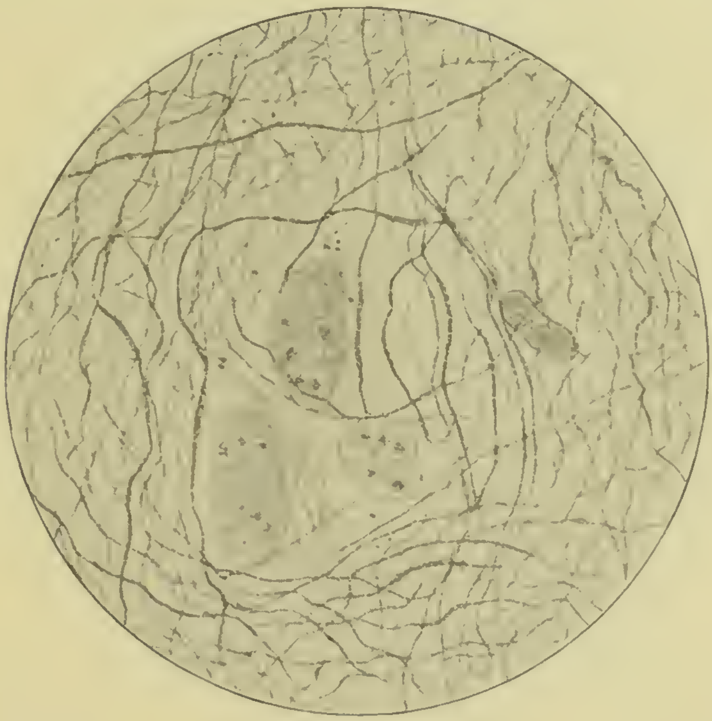


Fig. 2.—Meshwork of neuroglia fibers, some coarse, some fine. Four neuroglia nuclei, two of which are eccentrically placed in a distinct cytoplasmic body. In the cytoplasm of one of these is a "dot" near the nucleus.

neuroglia fibers often penetrate to a varying distance. Between these two types of cells are intermediate forms.

Tumor 1 shows greater complexity of neuroglia structure than the others. In tumor 2, with the same division into a large cyst and a solid portion, as in tumor 1, much less neuroglia is present. The solid portion of this tumor consists largely of small irregular cavities and spaces, into which project papillary processes covered by high cylindrical epithelium containing goblet-like cells. In this respect it resembles a papillary adenocystoma of the type which is very common in the ovary. Besides this structure, in a few places are small cysts whose walls are lined by neuroglia. Tumor 3

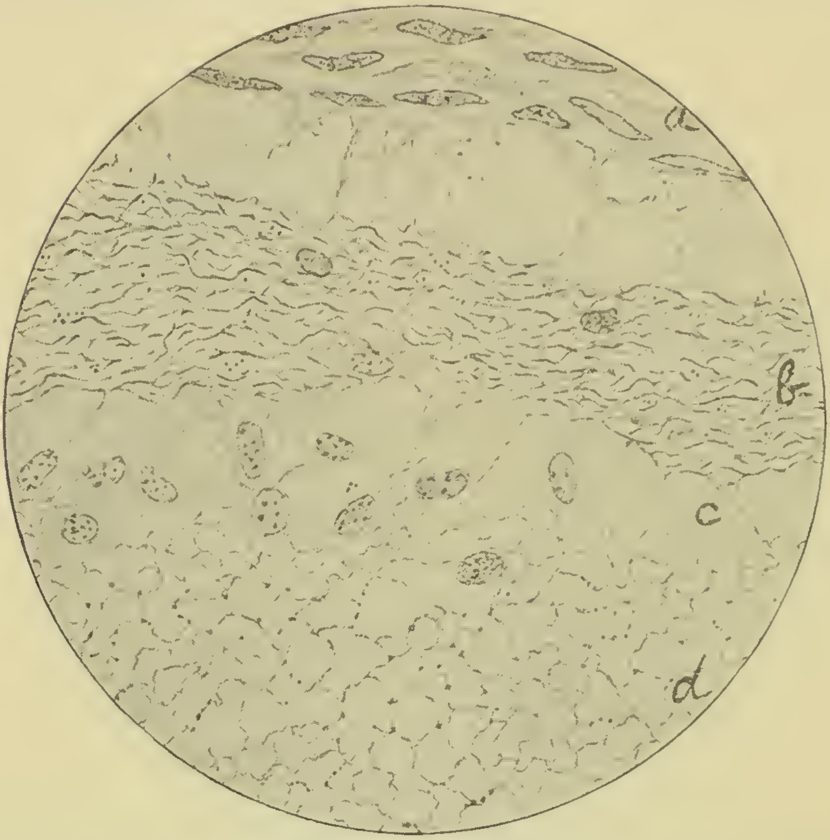


Fig. 3.—Neuroglia tissue. (*a*) Band of surrounding connective tissue. (*b*) Band of quite fine neuroglia fibers in general, running longitudinally and enclosing few cells. Between (*a*) and (*b*) there is a space due to shrinkage of tissue. (*c*) Layer of large neuroglia cells with eccentric nuclei. (*d*) Loose meshwork of fine neuroglia fibrils enclosing few cells. In this figure the dots represent cross sections of fibers.

shows numerous cysts, but the neuroglia tissue bears no close relation to these. It is sparingly present as small, irregular masses lying in connective tissue and sometimes abutting on a cyst.

In tumor 4 the neuroglia is present in relatively large masses. In one of these masses there is a central elongated cavity, which is not lined by epithelium. From this larger mass, bands of neuroglia extend into the surrounding tissue. In many places there is a very intimate intermingling of neuroglia and connective tissue fibers. In other places the two tissues are sharply demarcated. Tumors 4 and 5 each consist of a large cyst, whose wall is not very thick. In this wall lie small, rounded masses and elongated bands of neuroglia. In one of the tumors numerous corpora amylacea of irregular size and shape are present in the neuroglia tissue (Fig. 1). In tumor 6 a single mass of neuroglia measuring 3 to 4 mm. in diameter is seen.

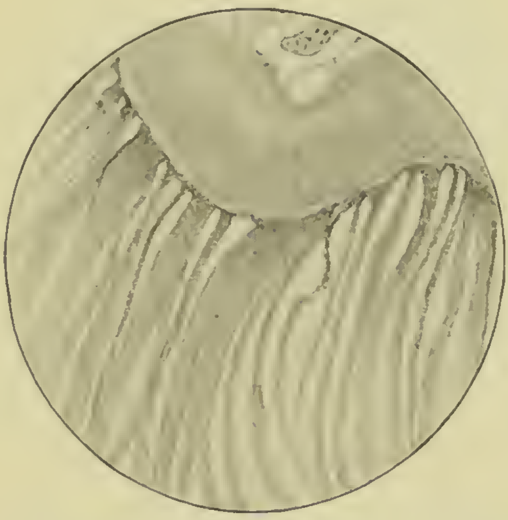


Fig. 4.—Coarse neuroglia fibers ending in an expanded foot adjacent to a hyaline band of connective tissue. From base of so-called rosette.

In the smaller neuroglia masses of all these tumors blood vessels are generally not present. In the larger masses they are found in moderate number and surrounded by a slight amount of connective tissue.

The appearance of the neuroglia in different areas is very various. The fibers differ in size and direction, the cells in form and frequency, and these differences are combined in an almost endless variety of ways. On the one hand we have masses of cells with but few fibers, on the other hand masses of fibers with infrequent cells. In neither extreme is the picture similar to that found normally anywhere in the central nervous system, though both resemble types of gliomata. The most frequent arrangement is a coarse irregular meshwork of fibers, some fine, some coarse, crossing each other in all directions (Fig. 2). Scattered among these fibers cells are rather infrequent.

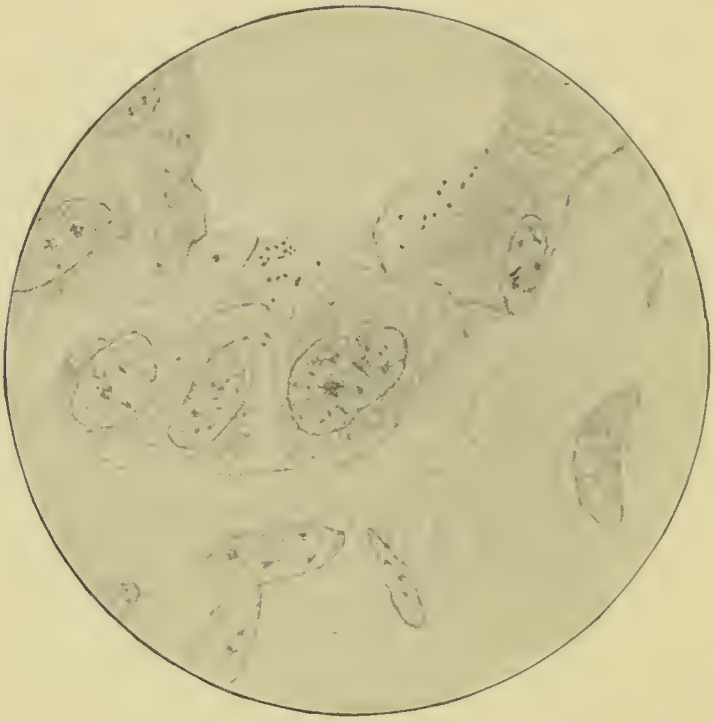


Fig. 5.—Part of a cyst lined by irregular cuboidal cells. In inner border of these are groups of "dots." In vicinity of cyst there is no neuroglia tissue. Section cuts cyst obliquely.

Instead of this arrangement, in many places, especially at the periphery of neuroglia masses, there is a more regular compressed meshwork of fibers having, in general, a parallel course (Fig. 3, b). Here nuclei are less frequent. Where these fibers are fine, the structure resembles that of the normal subpial and subependymal neuroglia.

A further modification in this direction results in bands of fibers, almost all of which run in the same direction and have practically a parallel course. In one or two instances these fibers are quite coarse and are interspersed with cuboidal cells roughly arranged in columns. This bears a slight resemblance to the arrangement of cells and fibers sometimes seen in tendons.

In places, instead of the interlacing fibers at first described, we have a finer meshwork of more delicate fibers and rather indefinite granular material, with nuclei widely scattered and generally having but little cytoplasm (Fig. 3, d). This arrangement of neuroglia fibers is similar to that found in many parts of the cerebral cortex.

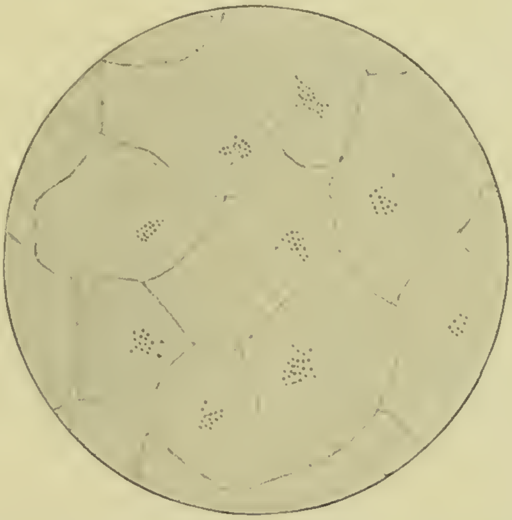


Fig. 6.—Groups of "dots" situated in the central end of cells lining a space. Section cut so as to give a view looking down on the top of the cells. Pale halo about some of the groups.

The individual neuroglia fibers do not vary in diameter in different parts of their course and do not branch. Different fibers vary greatly in size. Some are very fine, others coarse, and some appear as narrow bands. In many areas the fibers are of approximately the same size (Fig. 3). In some the fine and coarse are mingled together (Fig. 2). For most fibers no definite method of ending is apparent; they apparently end abruptly or pass from the level of the section. Some, like those in the so-called rosettes, to be described later, end by an expanded foot applied to connective tissue (Fig. 4).

The cells, like the fibers, present a variety of appearances. Many have rather small, deeply staining, round nuclei, about which little or no cytoplasm can be made out (Fig. 3, b). Some, on the other hand, have abundant cytoplasm, though when the cytoplasm is abundant the nucleus is apt to be larger, oval or slightly irregular, and vesicular (Fig. 3, c). The larger nuclei contain a distinct rounded chromatin mass, besides scattered fine granules. Some nuclei are elongated or even spindle-shaped; where they have a narrow cytoplasmic zone

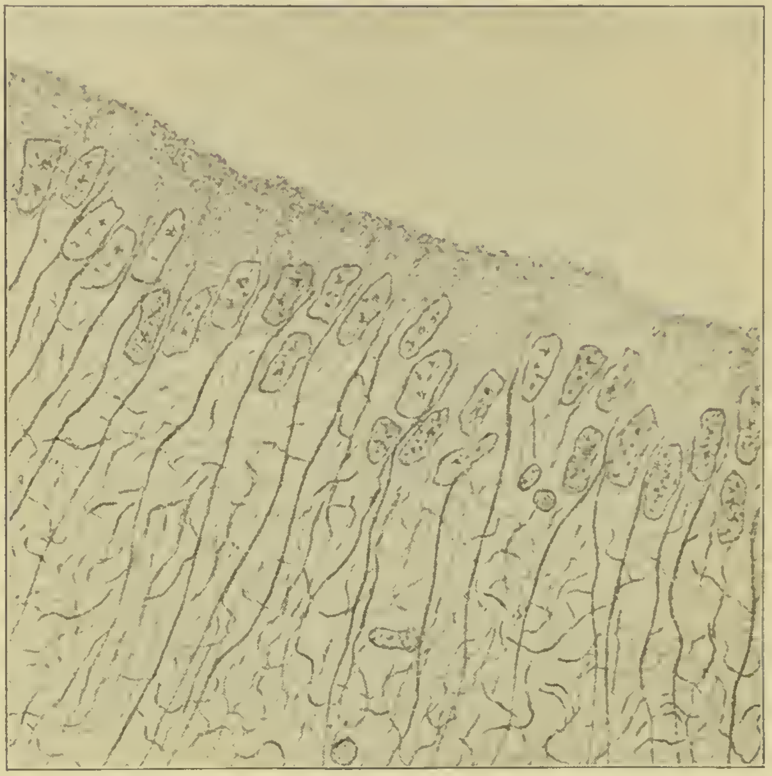


Fig. 7.—Ependymal epithelium lining a large space. Neuroglia tissue, with many rather coarse fibers perpendicular to ependymal layer and extending a short distance between the ependymal cells. From a preparation not stained by a method suitable for the demonstration of ependymal dots.

around them they resemble the cells of dense connective tissue. A few of the larger cells possess two or three nuclei. Sometimes the smaller cells are closely packed in a rich network of fibers. At other times the large cuboidal or irregular cells lie close together, separated only by an occasional fiber (Fig. 3, c). In some places the picture is one of closely packed polygonal or elongated epithelial-like cells, with very few intervening fibers.

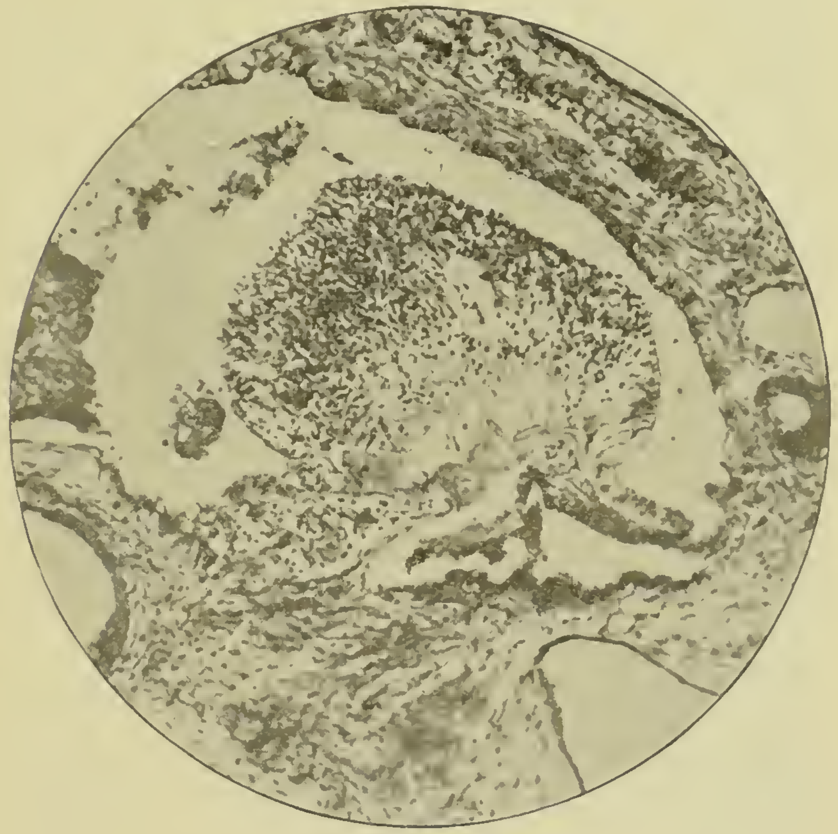


Fig. 8.—A simple rosette.

A number of the cells possess protoplasmic processes, but these are not very prominent. The fibers may be widely separated from the cytoplasm of a cell, and their closest relation appears to be one of contact, rather than of continuity. The cells have no cell membrane, and, whether round, oval, cuboidal, or irregular, their cytoplasm is rarely sharply demarcated, but gradually fades out at the periphery.

What is of particular interest is the presence in very many of the cells in the areas of neuroglia tissue of small dots, staining in the same manner as the neuroglia fibers. Often there is but one (Fig. 2). Sometimes there are two lying close together. Very frequently there are five to fifteen scattered in the cell or grouped together. They may have any position in the cell; sometimes they lie close to the nucleus, sometimes remote. Many times they are surrounded by a halo staining more palely than the general cytoplasm. Very rarely short rods, instead of dots, occur. These same dots occur also in the epithelium of the cysts of the first tumor. Here they occur in the inner border or between the nucleus and inner border of the cells (Fig. 5). They can be best seen when the section cuts the cyst so that a view of the top of the cell is obtained (Fig. 6). The cysts which these cells line vary in size. They may be minute, representing a small space or lumen in a group of cells, or they may be large. The cysts may have neuroglia in close proximity, or none be adjacent. In some cysts neuroglia fibers penetrate between the lining cells (Fig. 7). Of these cells some are low and cuboidal, and others high and cylindrical. Not infrequently in ciliated cells rows of these dots are situated at the base of the cilia. In others they are not present.

In tumor 1 are peculiar structures which deserve attention from their vague resemblance to retina and from their containing fibers which stain like neuroglia fibers. These partially fill some of the cysts. In their simpler form they consist of a rounded mass with a pedicle but little smaller than the mass (Fig. 8). The outer portion of this mass is made up of closely packed round or oval nuclei, sometimes deeply staining, sometimes vesicular with one to three rounded chromatin masses. The cytoplasmic bands of these cells are ill-defined, and between some of them fibers staining like neuroglia fibers can be traced. As the central and basal portions are approached there are fewer nuclei and more fibers. At

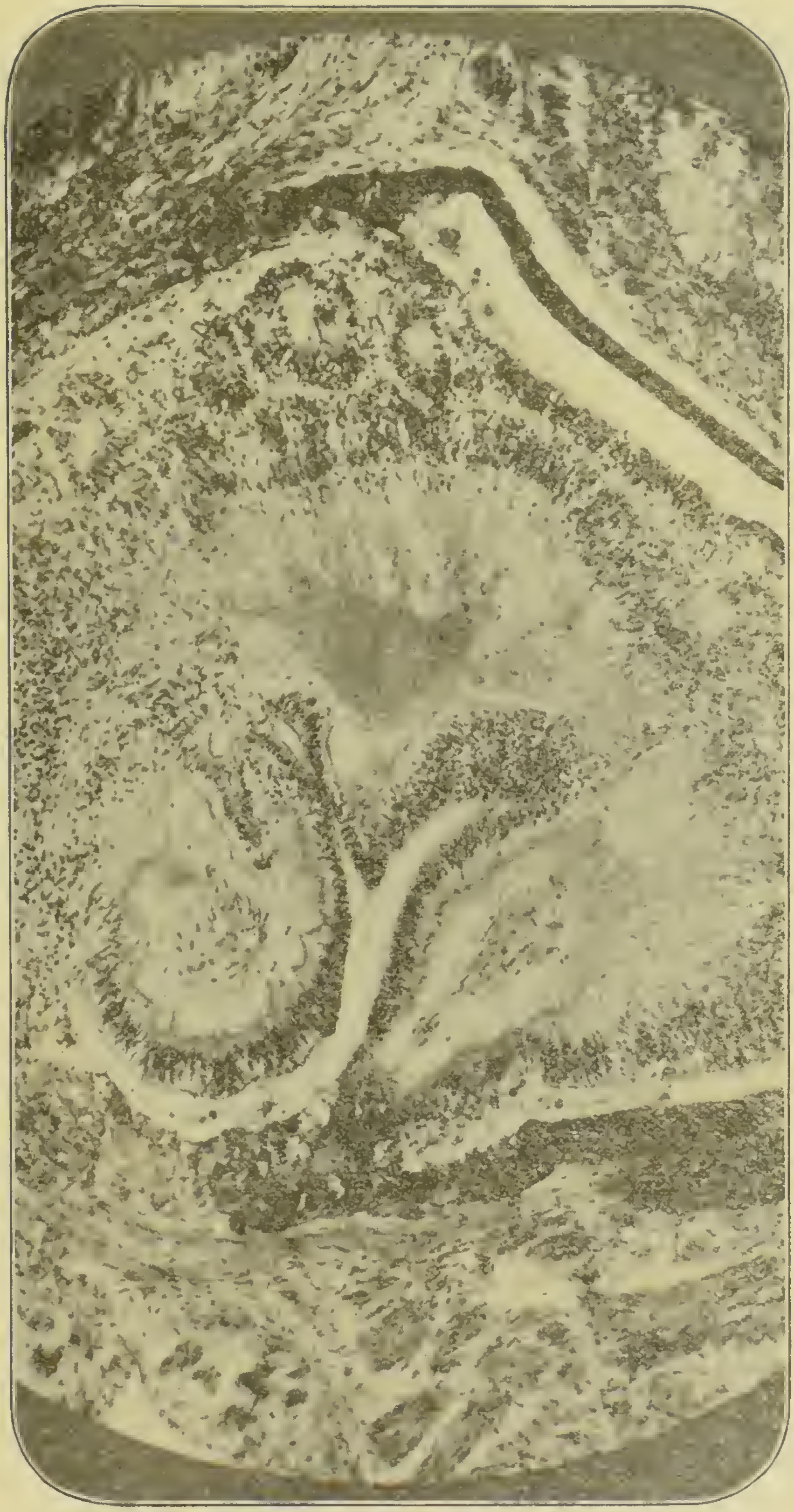


Fig. 9.—A more complicated rosette.

the base there are almost no nuclei and many coarse fibers (Fig. 4). Most of these coarse fibers are parallel in direction and end against connective tissue by a fairly definite expanded foot. The connective tissue in this portion is frequently in the form of a hyaline band (Fig. 4), sometimes gently undulating, sometimes quite convoluted. Instead of this band there sometimes is a mass of indefinitely fibrillar or ill-defined hyaline connective tissue. In the region of the base there is always a layer of high cylindrical epithelium which passes by gradual transition into the epithelium lining the cyst. The ingrowth and fusion of several such masses produce more complicated structures (Fig. 9). The cysts in which they occur are almost always partially or completely lined by epithelial cells, which are filled with

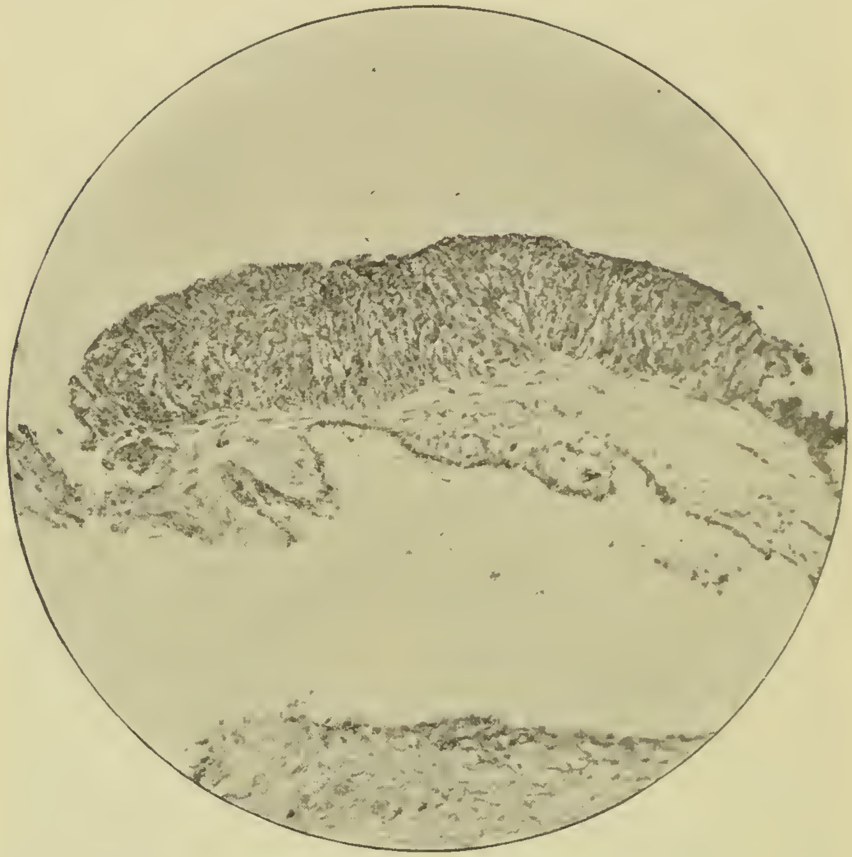


Fig. 10—Early stage in formation of so-called rosette—a local thickening of epithelium of a cyst with formation of fibers between cells.

fairly coarse granules of brown pigment. This pigment resembles that found in the retina. The structures themselves resemble in many places the rosettes of gliomata retinæ, and, for need of a better word, may be called rosettes. They have similar small, round nuclei. The coarse neuroglia fibers ending in apposition to a connective tissue band suggest the fibers of Müller. Their occurrence in cysts lined with pigmented epithelium adds further to the analogy.

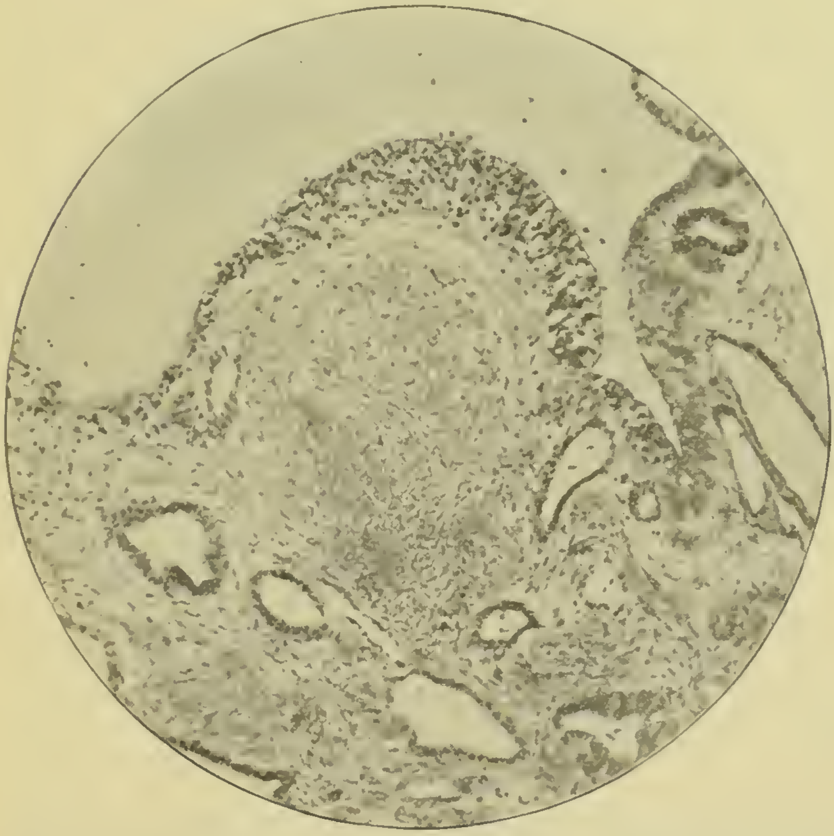


Fig. 11.—Beginning of pushing forward of epithelium by connective tissue formation at base.

The mode of development of the structures described above can apparently be traced. At first there is a proliferation of the epithelium at one point in a cyst, resulting in a thickened layer of cylindrical cells, between which fibers staining like neuroglia appear (Fig. 10). The fibers and cells increase in number, and at the same time the connective tissue proliferates and pushes the mass into the cyst cavity (Figs. 11 and 12). The fibers grow mainly toward the base, while the cellular portion remains toward the center. In some cysts several such ingrowths are found (Fig. 13), and it is probable that in this way the more complicated masses are formed. Many variations in complexity are seen, and forms representing different stages of development appear in the various sections.

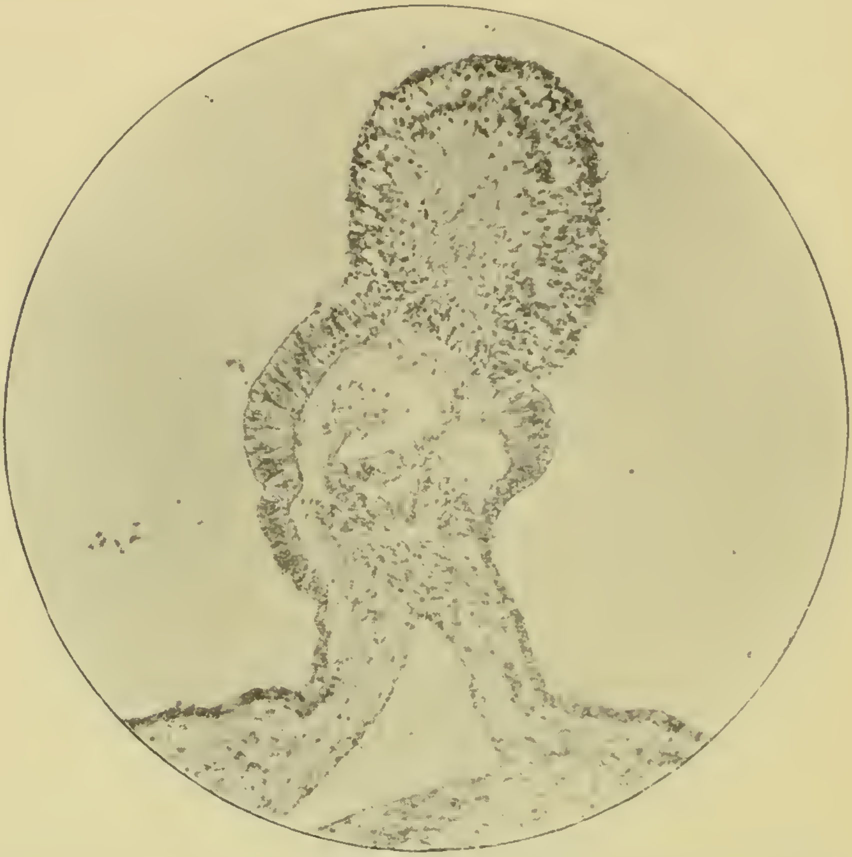


Fig. 12.—More definite pedicle of connective tissue capped by mass composed of cells and fibers.

Discussion.—Nowhere in the central nervous system do we have such an intimate intermingling of neuroglia and connective tissue as in these teratoid tumors. In the brain and cord the separation between pia and cortex is usually sharp. Gliomata, as a rule, are in juxtaposition to surrounding white or gray matter or to pia, and so do not lie in very intimate contact with mesoblastic tissues. The nearest approach to these conditions is where vascular radicles, accompanied by a small amount of connective tissue, penetrate nerve tissue from the pia, and where the connective tissue of the choroid plexus abuts on neuroglia. In case of the teratoid tumors this mingling of the two tissues often occurs at points where no vascular radicles penetrate, but seems due rather to a coincident growth of adjacent foci of two tissues of different germ layer origin, with an overlapping, due to irregularity in rate of development. Such an explanation seems more plausible than that we have the one tissue invading preformed tissue of the other kind in the way a malignant tumor invades adjacent structures.

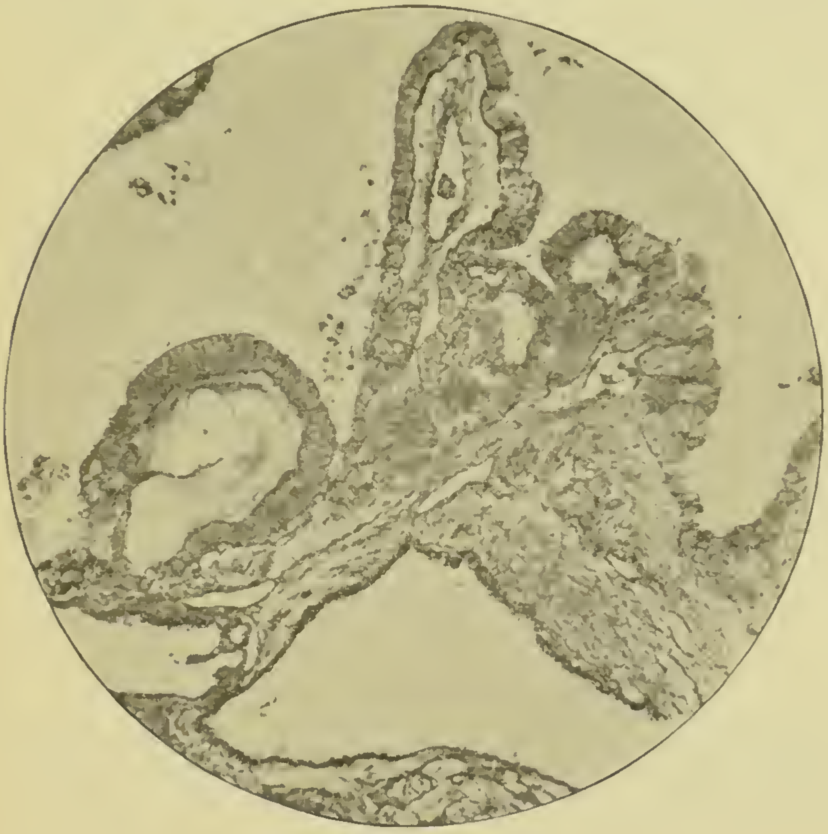


Fig. 13.—Several ingrowths into a cyst.

Moreover, there are present fibers in connective tissue remote from definite neuroglia masses. These stain in a manner identical with the neuroglia fibers of the larger masses, and in size, absence of branching, and undulating course present no differences from many fibers seen in them and in gliosis and gliomata. Their isolated presence in connective tissue seems difficult of explanation. At first it was assumed from their staining properties that they were to be considered of undoubted neuroglia origin. It was thought that their presence in connective tissue might be explained by their arising as an offshoot from a neuroglia mass, with which they were originally connected, and from which later in the growth of the connective tissue they had become separated. Another possible explanation is that early in the development of the tumor a small group of neuroglia cells became separated in the midst of connective tissue elements, formed their specific intercellular substance and then disappeared. Either theory would explain their present position, assuming that they are true neuroglia fibers, that is, fibers formed by neuroglia cells. Of this we have no proof, except the morphology of the cell, the relation of the fiber to the cell and the

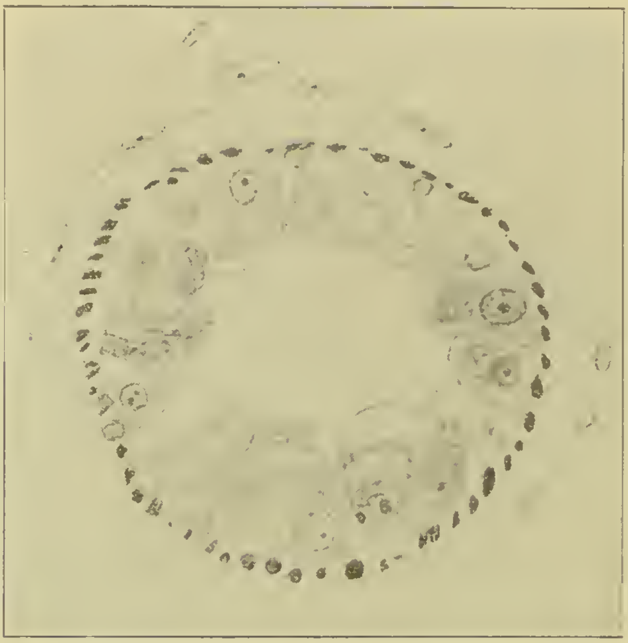


Fig. 14.—Sweat duct in teratoid tumor, showing cross section of coarse longitudinal fibers lying between true basement membrane and epithelial cells. These stain with neuroglia stains.

staining reaction of the fiber. The former, in many cases, is by no means definite, and in this connection no cell resembling neuroglia cells are present. Doubt as to the latter arose from the following: In some of the teratoid tumors, in which no neuroglia occurs, there are present about sweat ducts fibers staining in the same way as neuroglia fibers, with both the phosphotungstic acid hematoxylin and modified fibrin methods (Fig. 14). While these studies were in progress, Dr. Mallory, investigating connective tissue and smooth muscle, found fine fibers which stain red by the acid fuchsin potassium permanganate method, in sharp contrast to very abundant unstained fibers. This method also stains sharply true neuroglia fibers, and suggests a possible further resemblance in staining reaction between neuroglia and certain connective tissue fibrils.

To test this analogy three specimens of carcinoma of the breast, in whose stroma Dr. Mallory had found the red staining fibrils very abundant, were fixed in either formaldehyd or alcohol. To these were applied the phosphotungstic acid hematoxylin, modified fibrin, Benda's and Huber's methods of staining neuroglia. With all of these fibrils were found, which, from their holding the stain and, to a certain degree, their relation to cells, might be confused with neuroglia. From this it is evident that there are connective tissue fibers which do not readily decolorize after these staining methods and whose identification can not be based solely on staining reaction, since they at times stain in a manner similar to neuroglia fibers.

From this evidence it appears that the fibers scattered in the connective tissue of the teratoid tumor staining in the same way as neuroglia are not of necessity of neuroglia origin. Their true nature at present is indeterminate. In some places they are probably neuroglia, in others not.

Dots, staining in the same way as the neuroglia fibers, have been described as occurring in many of the cells of these tumors. The question as to their significance naturally arises. Similar dots or short rods have previously been described by Weigert in the normal ependyma,[8] by Storch in cells lining small spaces of a glioma,[9] by Benda,[10] by Mallory,[11] and by Lewy,[12] in the neuroglia cells of gliomata and by myself[3] in a teratoma (tumor 1 of this report), both in the cells lining cysts and those scattered among neuroglia fibers. Various meanings have been attached to them. Weigert in his first paper regarded them as an interrupted cuticular layer. Mallory considered the dots as possible evidence of the ependymal origin of the gliomata studied by him. I, concurring in this view, attached a similar import to their presence in a teratoma. Lewy looked on them as centrosomes, but regarded the presence of groups of them in neuroglia cells as an inheritance from ancestral ependymal cells, and the ring or rosette arrangement of some as a probable rudimentary cilia formation. In considering the different views, certain facts have been brought out which do not readily harmonize with them, though at the same time it has not been possible to determine definitely the nature and significance of these dots, and the attempt to advance any new hypothesis regarding them will not be made.

The earlier view of Weigert that they are a cuticular arrangement no longer seems tenable since the dots are found irregularly scattered through the cytoplasm of cells lying in the midst of large areas of neuroglia fibers and lining no space or lumen.

---

[8] Weigert: Bemerkungen über das Neurogliagerüst des menschlichen Centralnervensystems, Anat. Anzeiger, 1890, v, 543.

[9] Storch: Ueber die path. anatomischen Vorgänge am Stützgerüst des Centralnervensystems, Virchow's Arch. f. Path. Anat., etc., 1899, clvii, 127 and 197.

[10] Benda: Path.-anatomische Bemerkungen zu dem zweiten vorstehenden Fall A. Fraenkel's, Deutsch. Med. Woch., 1898, 476.

[11] Mallory: Three Gliomata of Ependymal Origin; Two in the Fourth Ventricle, One Subcutaneous Over the Coccyx, Jour. of Med. Research, 1902, viii, 1.

[12] Lewy: Ueber Centralkörperchen in Gliomen, Virchow's Arch. f. Path. Anat., etc., 1903, clxxi, 236.

Are they centrosomes? They can be stained by methods used for demonstrating centrosomes as the iron hematoxylin method. Multiplicity of centrosomes has been described by Heidenhain in bone marrow giant cells. We have studied these dots in the ependyma of a series of pig fetuses from 18 mm. to 17½ cm. in length, and in several early human fetuses, using the phosphotungstic acid hematoxylin staining method. Here they are almost always present as a row or group adjacent to the spinal canal or ventricle. At this time nuclei are situated generally at some distance from the central space and its bordering dots, and dots are not found except in this arrangement. Mitoses of the cells in this region are common, and the dividing nuclei often approach near the space at whose border the dots are grouped. Yet there is no apparent change in the dots, nor are any dots seen associated with the mitoses. This does not seem to favor the view that the dots are centrosomes.

That they bear no close relation to the formation of neuroglia fibers, whose staining reactions they have, is shown by their presence in the fetuses studied at a time much before the fibers show any evidence of their presence.

The dots are already present in an 18 mm. pig, when, according to Hardesty,[13] differentially staining neuroglia fibers appear first in pigs from 16 cm. to 21 cm. in length.

The dots do not appear to be closely associated with cilia, since they were absent in some ciliated cells, and occurred in some non-ciliated cells. They are not always present in cells which originate from ciliated cells, as they could not be demonstrated in an adenocarcinoma of the uterus.

Can the presence of these dots be considered evidence of the ependymal character and ancestry of a cell? Dots were not found in most parts of these tumors except in neuroglia cells or cells lining cysts, and presumably of ependymal character. They were not found in several carcinomata of the breast or in a malignant adenoma of the large intestine. Dots very similar were found in the high cylindrical epithelium of that part of one tumor described as resembling a papillary adenocystoma of the ovary. Dots similar, but slightly larger, were found in some sweat ducts in these teratoid tumors and in those of a specimen of normal skin. Larger granules staining similarly with Mallory's phosphotungstic acid hematoxylin were found in the pancreas, but dots were not present in the kidney of this case, nor were they found in the fetal organs of the 18 mm. pig. This shows that dots, if not identical with those occurring in true ependyma, yet staining similarly, occur in cells undoubtedly of different nature, and so the mere presence of such dots in a cell or group of cells can not be considered diagnostic of the ependymal character and origin of these cells. When they do occur in cells which offer other evidence of a central nervous system origin, it seems justifiable to regard their presence as adding evidence in favor of the view that the cells containing them bear a genetic relation to ependyma. This is true for cells which line cysts and are in close relation to neuroglia tissue and for cells which are embedded in neuroglia fibers. Where the cells line cysts and bear no close relation to neuroglia, such a conclusion does not seem justified, and their nature remains undetermined.

---

[13] Hardesty: The Neuroglia of the Spinal Cord of the Elephant with Some Preliminary Observations on the Development of Neuroglia Fibers, Am. Jour. of Anat., 1902, ii, 81.

CONCLUSIONS.

From the preceding work the following conclusions may apparently be drawn:

1. Neuroglia is a common constituent of teratoid tumors.

2. Its structure in them is very varied, simulating many known forms.

3. Neuroglia is more intimately associated with mesoblastic tissues in teratoid tumors than elsewhere.

4. In such tumors occur isolated fibers and groups of fibers which stain like neuroglia, but whose nature can not be determined by the staining reactions of Mallory, Huber and Benda, since these methods may stain other fibers than neuroglia fibers.

5. In many cells of these tumors occur small dots or groups of dots which have similar staining reactions to neuroglia fibers.

6. The presence of these dots in cells, though not absolutely diagnostic, may be considered as evidence in favor of the ependymal origin of the cells in which they occur.

Finally, it is with great pleasure that I acknowledge the very many valuable suggestions made by Dr. F. B. Mallory and his interest in this study. To Dr. J. A. Sampson of the gynecologic department of the Johns Hopkins University I am indebted for a number of these tumors, and to Dr. W. H. Lewis of the anatomic department of the same institution for the series of fetal pigs.

DISCUSSION.

Dr. L. Hektoen, Chicago—Are the rosette bodies which you have described to be regarded as imperfectly developed eyes?

Dr. H. A. Christian, Boston—The analogy of these structures to eyes was considered and there is a great deal in favor of this view. The occurrence in many of these cysts of pigmented epithelium, the fibers which suggest Müller's fibers, and the small round nuclei which are very common in imperfectly formed retinæ, are all in favor of that theory; but there is no proof of what they are, and this is a mere opinion. However, I regard them as possibly an attempt to form eyes.

THE MORPHOLOGY AND BIOLOGY OF THE PARASITE FROM A CASE OF SYSTEMIC BLASTOMYCOSIS.

F. J. OTIS, M.D.
Instructor in Bacteriology and Hygiene, and
NEWTON EVANS, M.D.
Instructor in Pathology, American Medical Missionary College.
BATTLE CREEK, MICH., AND CHICAGO.

The observations recorded in this paper were made on the parasites obtained in the tissue and by artificial culture from the case of fatal systemic blastomycosis reported by Ormsby and Miller.[1] We wish here to acknowledge their assistance in the work done and kindness in allowing us to use the material from their case.

In May, 1894, Gilchrist[2] described in tissues from a skin lesion the spherical, double-contoured, budding microörganisms which have since been observed in about thirty-five reported cases. In this case cultures were not made and little was known of the biology or nature of the parasite. In November of the same year Busse[3] reported a case of systemic infection resulting fatally in which a similar parasite was described as the etiologic factor. Cultures were made from this case and the organisms extensively studied by Buschke.[4] In culture the organism grew by budding, and mycelial formations were also seen.

---

[1] Ormsby, O. S., and Miller, H. M.: Report of a Case of Systemic Blastomycosis with Multiple Cutaneous and Subcutaneous Lesions, Jour. Cutan. Dis., March, 1903.

[2] Gilchrist, T. C.: Communication to the American Dermatological Association, May 30, 1894.

[3] Busse, Otto: Ueber Parasitare Zelleinschlusse und Ihre Zuchtung, Centralbl. f. Bakt. und Parasitenk, 1894, xvi, 175; also, Ueber Saccharomycosis Hominis, Virchow's Archiv, 1895, cxl, 23; also, Experim. Untersuch. Ueber Saccharomycosis, Virchow's Archiv, 1896, cxliv, 360; also, Die Hefen als Krankheitserreger, Berlin, 1897.

The cases reported have had lesions for the most part confined to the cutaneous surface. A few cases of systemic infection, however, have been observed. The cases have largely occurred in the United States. The largest number have been observed in and about Chicago. The cutaneous lesions have characteristics which show such uniformity that they may be distinguished often by their gross appearance. The microscopic findings are similar in all cases, and the presence of the typical organisms in the tissue, or pus of miliary abscesses, is pathognomonic. The cases of systemic infection, as far as we can determine, which seem to have definite confirmation, are four: First, the case of Busse and Buschke; second, a case reported by Montgomery and Ricketts,[5] and later by Walker and Montgomery;[6] third, one reported by Ophüls and Moffit[7] (San Francisco), identical with those cases which have heretofore been called a protozoan infection, but which was proved by him to grow as a typical fungus in artificial media; and lastly, the case of Ormsby and Miller,[1] in Chicago, from which our material was obtained. All of these systemic cases have resulted fatally.

There is much uniformity in the morphology of the organism, as found in the tissues and purulent exudate, in all these cases, both cutaneous and systemic. They are spherical or oval, double-contoured, with very refractive cell capsule, increase by budding, and, in the

---

[4] Buschke, A.: Ueber Hefenmykosen bei Menschen und Thieren, Volkmann's Samml. Klin. Vortrage, 1898, No. 218; also Ueber Hautblastomykose. Verhandl. der Deutschen Dermatologischen Gesellschaft. Sechster Congress, 1899, 181.

[5] Montgomery, F. H., and Ricketts, H. T.: Three Cases of Blastomycetic Infection of the Skin; One Case Limited to "Tumor" of the Lower Lip, Journal Cutan. and Genitourinary Diseases, January, 1901.

[6] Walker, J. W., and Montgomery, F. H.: Further Report of a Previously Recorded Case of Blastomycosis of the Skin; Systemic Infection with Blastomyces; Death; Autopsy. THE JOURNAL A. M. A., April, 5, 1902.

[7] Ophüls, W., and Moffit, H. C.: A New Pathogenic Mould. Phila. Med. Jour., June 30, 1900.

Ophüls' case by sporulation, which has not been definitely proved in any other case. No mycelia are found in the tissues or pus. The size varies within wide limits in different cases, parasites from three to thirty microns in diameter being seen. The cultural characteristics of the organisms from different cases show marked variations, in some cases multiplying by budding exclusively, in others growing mycelia principally, and in others abundant aërial hyphæ are produced. Hektoen[8] describes very minute forms which, under proper conditions, develop into the larger form. And, further, some of the organisms, if watched for some time through a number of generations of growth, completely change in their characteristics on artificial media, multiplying at one time by gemmation, and afterward forming mycelia, or vice versa. We may thus say that in its growth and cultures, polymorphism is manifested to a striking degree. Hektoen made a careful study of the parasites from a case of blastomycetic dermatitis.[8] He describes the appearance of the different forms of the organism as seen in the tissues; some with a clear zone surrounding the protoplasm inside the capsule, others in which this is inconspicuous; some with large vacuoles in the protoplasm, others with dense, granular protoplasm without vacuoles. He also describes mulberry-like masses of hyaline bodies in the tissues, both intracellular and extracellular. The cultural forms varied much in size, a small, coccus-like form being described.

Gilchrist[9] makes extensive observation on the morphology and biology of the parasite. The process of budding, as it occurs in the tissue, is accurately followed. The endosporium, or protoplasm, of the bud increases to almost the size of the parent, and then becomes separated. He also notes peculiarly refractive forms which will not take the stain. Other forms in which the protoplasm has contracted into a half-moon shape are described. The adult forms in cultures show in the protoplasm fine, deeply-staining granules, larger refractive granules, and often one or more vacuoles.

---

[8] Hektoen, L.: The Organism in a Case of Blastomycetic Dermatitis, Jour. Exper. Med., vol. iv, 1899.

[9] Gilchrist, T. C., and Stokes, W. R.: A Case of Pseudo-Lupus Vulgaris Caused by a Blastomyces, Jour. Exper. Med., vol. iii, No. 1, 1898.

Ricketts[10] has collected and tabulated observations concerning the morphologic, biologic and cultural characteristics of the organisms from a number of cases (seventeen), from which table he concludes that there are three more or less distinct groups of organisms having common generic characteristics. Montgomery[11] gives a very careful description of the clinical, pathologic and bacteriologic features from thirteen recorded cases.

DESCRIPTION OF CASE.

The clinical history and discussion of the present case have already been reported by Ormsby and Miller,[1] accompanied by a brief description of the microscopic and gross pathology of the tissues affected, and also a short study of the cultural characteristics of the organism by the present observers. The history indicated that the primary infection was located in the pulmonary tissue, followed by the cutaneous and subcutaneous lesions. Practically all the cutaneous lesions were of such a nature as to indicate the hemal origin of the infection, the superficial tissues being affected only after the process progressed from the deeper tissues. One lesion only, on the hand, had the characteristics described in the lesions of blastomycetic dermatitis of local origin. Of the internal organs, the lungs were most extensively involved; grayish nodules of varying size, and in enormous numbers, being distinguished in all parts of the tissue of both lungs. The pleuræ were extensively affected, and adhesions and whitish nodules of varying size were present in all portions. The lesions in the spleen were almost as extensive as in the lung. The nodules composed of typical organisms were found also in the liver, kidneys, pancreas, trachea and larynx. (This is apparently the first case in which involvement of a mucous membrane proper has been described.) The teased specimens in hanging drop from the different organs gave abundant opportunity for studying the living parasites as they occurred in the lesions. The stained sections from the lung tissue, especially, show parasites in immense numbers.

---

[10] Ricketts, H. T.: Oidiomycosis (Blastomycosis) of the Skin and Its Fungi, Jour. Med. Research, vol. vi, No. 3.

[11] Montgomery, F. H.: A Brief Summary of the Clinical, Pathologic and Bacteriologic Features of Cutaneous Blastomycosis, THE JOURNAL A. M. A., 1902.

MICROSCOPIC APPEARANCE OF TISSUES.

Lung.—The slight degree of inflammatory reaction is noteworthy, the lesions being composed almost entirely of the parasites. There is some newly-formed connective tissue containing small round cells, polynuclear leucocytes and many mast cells, the protoplasmic granules of which stain red with polychrome methylene blue. There is some coagulation necrosis, areas of caseation appearing mostly at the center of the nodules. In the areas where the parasites are very abundant the elastic tissue has entirely disappeared, as indicated by staining with orcein. The epithelial cells which are remaining in the lung are largely detached, and are remarkable for the amount of brownish pigment granules which they contain. Similar deposits of pigment are found in many other cells, especially the polynuclear leucocytes of the blood.

The giant cells in the lung tissue are remarkable for their number and size. They vary from twenty microns to many times that diameter. They all contain parasites in different stages of development, and the larger ones are crowded with them, the cell nuclei being few and indistinct, while in the smaller giant cells the cell nuclei are numerous and prominent. The peripheral arrangement of the nuclei seen in the tubercular process is not followed, but many of the nuclei are near the center of the cell body.

Spleen.—The splenic tissue is riddled by the growth of the typical organisms, showing grossly as yellowish-white areas and nodules. Microscopically, the parasites are seen scattered widely throughout the tissue, but not in such large masses as in the lung tissue. The splenic pulp contains much brown pigment.

The lesions of the kidney, liver and pancreas are smaller and less numerous, often escaping naked eye examination. The immense numbers of parasites and small amount of newly-formed connective tissue are the principal characteristics of these lesions. In and about them are always seen typical mast cells.

Lymph Nodes.—The peribronchial lymph nodes were markedly enlarged, and contained large amounts of black pigment, apparently carbon. On microscopic examination we were unable to demonstrate the presence of any parasite in the tissues; however, in one section parasites were seen in the blood stream of one of the vessels.

MORPHOLOGY OF PARASITES IN THE TISSUES.

The stained sections of lung tissue offer excellent opportunity for a study of the parasites in different stages of their development. There are seen large, rounded masses of parasites under the microscope (Fig. 1), at the center of which the organisms are all of large size, take very little stain, show few buds, and many contain large vacuoles, occupying almost the entire cell. These are evidently old cells which are degenerating and disintegrating, as indicated by the granular detritus among them. At the periphery of these areas the organisms differ much from those at the center. The cells are of various sizes, have deeply-staining protoplasm and are undergoing cell division actively. These areas, therefore, give excellent opportunity for the study of the life history of the parasite in the tissue.

The most satisfactory stain which we have found for studying the structure of the yeast-like organism is the polychrome methylene blue stain, applied according to Unna's method. Other stains used are hematoxylin and eosin, methylene blue and eosin, Gram's stain, Van Giesen's method, carbol fuchsin and orcein.

The typical parasites are of various sizes, measuring from five to fifteen microns in diameter. They all have a definite, refractive capsule, which takes most stains sparingly, usually less than one micron in thickness. The capsule stains best by methylene blue and eosin. Within the capsule the structure has so many variations as to be almost picturesque in the variety of forms seen.

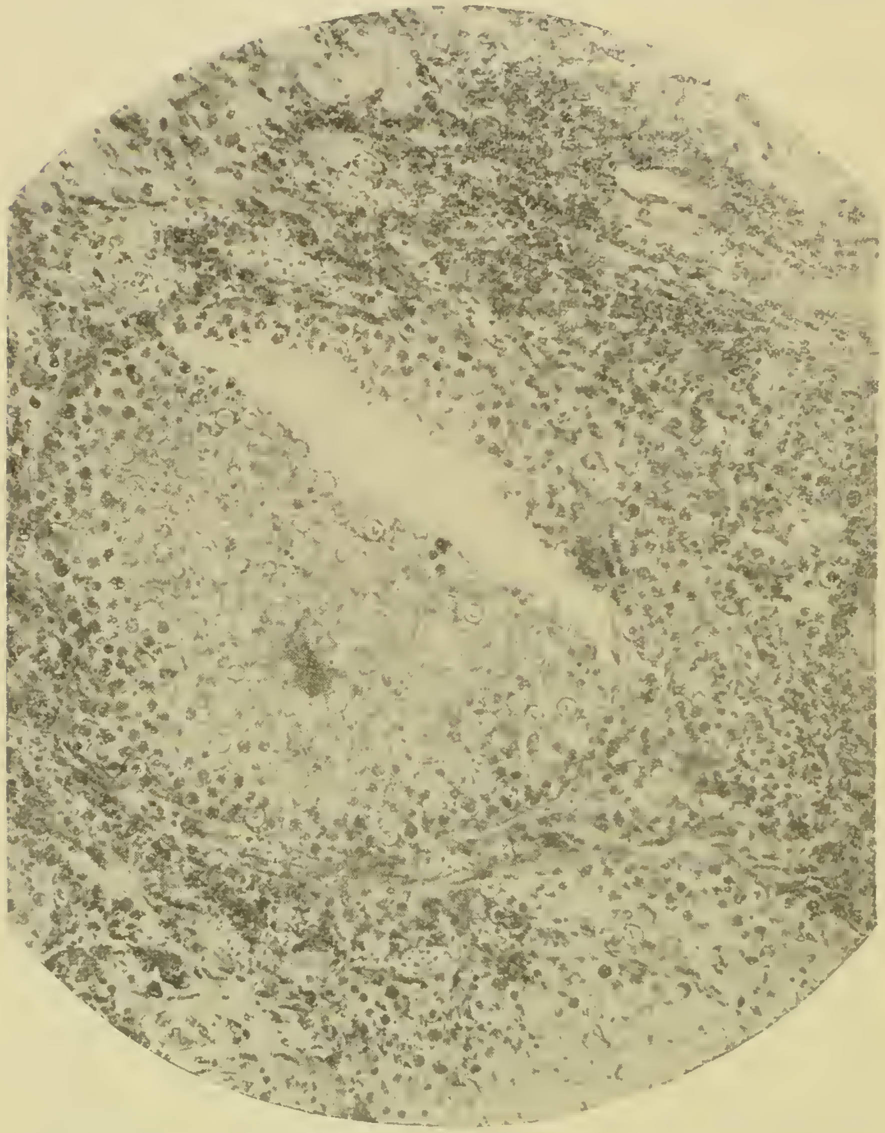


Fig. 1.—Nodule of blastomycetes in lung tissue. Center showing old, poorly-staining organisms, and periphery showing young, deeply-staining organisms.

Many of the cells have a wide, clear zone within the capsule and surrounding the protoplasm.

In the natural order of growth of any organism, one expects to find a certain definite order of development, and it has been our effort by careful study of the various forms to determine the characteristics of the cells at the different stages of their development. We see, then (Fig. 2), in all forms a capsule protoplasm of varying structure and staining properties; in many the clear space between the capsule and protoplasm, and many contain one or more vacuoles of various sizes. Budding forms are numerous, and cells of almost all types of structure are seen undergoing this form of multiplication; but the budding process is most active in cells of a certain type—those in which the protoplasm is dense, deeply staining and relatively small in amount, being surrounded by a wide, clear zone. These are of medium or small size generally, and are evidently relatively young and actively growing forms. We can distinguish, then, the following types:

1. Cells which are small in size, from five to ten microns usually, having a relatively small mass of deeply-staining protoplasm, surrounded by a wide, clear zone inside the capsule. The mass of chromatic substance is spherical, except in those which are undergoing the budding process, is centrally or excentrally located, is finely granular or homogeneous, but very deeply stained. Many of these are budding.

2. Forms similar to the first, but slightly larger on an average, the deeply staining protoplasm being more coarsely granular and containing clear, rounded spaces, which are evidently vacuoles, of varying size and number. The protoplasm occupies a larger area in the cell, the clear zone being narrower than in the preceding form. Many of these are undergoing the budding process.

3. Forms similar in size to the preceding, protoplasm staining well, granules large, a few large vacuoles being

present, all of the space occupied by the protoplasm, the clear zone being obliterated or inconspicuous.

The preceding forms are found especially at the periphery of the circular masses of parasites described in the lung tissue, and are evidently younger and growing forms, actively dividing.

4. Large cells in which the protoplasm fills the capsule and contains a single, very large, spherical vacuole, centrally or peripherally located. The protoplasm thus appears as a ring of granular material, does not take a deep stain, and some small, circular, hyaline areas are seen in it. These forms are seen mostly at the center of the masses of parasites.

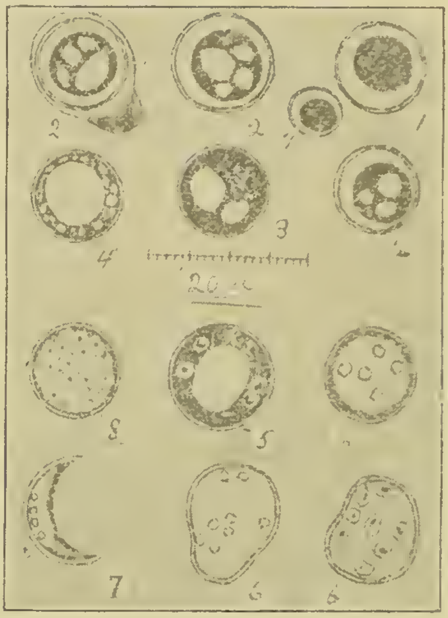


Fig. 2.—Diagrammatic representations of adult forms of parasite showing different stages of development. (Made from drawings.) 1. Young forms, dense protoplasm, wide clear zone. 2. Protoplasm vacuolated; one enclosed by tissue cell. 3. Protoplasm fills capsule. 4. Contains one large vacuole. 5 and 6. Contain spore-like bodies. 7. Collapsed form; one extracellular spore-like body. 8. No vacuole; protoplasm transformed into spore-like bodies.

5. Large forms with very large central vacuole, a thin layer of protoplasm which has undergone division into spore-like bodies, which have the appearance shown in the figure. These bodies are about one micron in diameter, appear to have a central clear space surrounded by

a ring of chromatic substance of irregular thickness, the chromatic substance often being accumulated at one portion of the ring, at other times appearing as two masses on opposite sides of the ring. These spore-like bodies are seen to be only at the periphery of the cell capsule. These forms of cells are found only at the center of the masses of parasites.

6. Similar cells in every respect, except that they are collapsed, the fluid contents of the vacuole having been evacuated. These forms are evidently derived from those described in paragraph No. 5. Very few of those cells with refractive contents have undergone any such change.

7. Another distinctive form appears in which the protoplasm contains no large vacuole whatever, but as they develop the protoplasm divides into from ten to fifteen small hyaline bodies, in many of which is seen a central densely staining body. Similar bodies to these are also seen outside the capsule.

Other variations in the structure of the cells may be seen—some with refractive contents which does not take the stains; others are seen in small numbers in which the protoplasm is completely obscured by a mass of brown pigment. The presence of these forms is possibly an explanation of the origin of the pigment granules described in the tissue cells, and in the leucocytes of the blood. With polychrome methylene blue stain a great many of the organisms contain in their protoplasm basophilic granules staining red. These have been described by Gilchrist and others. There is a remarkable variation in the affinity which different organisms have for the stains, cells lying side by side, and apparently of the same structure, show an entirely different reaction to the stain. Several observers have described adventitious capsules. We have not observed a similar condition, but often individual parasites are seen within the protoplasm of the tissue cells, which is stretched about it and so attentuated as to resemble a capsule.

SPORE FORMATION.

Multiplication of the organism by budding is the usual method within living tissue, and by budding and mycelial and conidial formation in the culture, but the production of endospores and propagation by their development is still a matter of doubt. In the case under consideration the findings in the tissue seemed to indicate the presence of spore formation, and we will endeavor to describe this process here (Fig. 3). These forms occur for the most part in the centers of the masses of parasites where all the organisms are of advanced age, and many are disintegrating. Most of the cells in question contain large central vacuoles, the protoplasm being pushed to the periphery, appearing as a ring just within the capsule. This ring of protoplasm has undergone division into bodies which are small (about one micron in diameter), and are composed of an outer ring of chromatic material and a hyaline center (Fig. 4). These bodies have already been described in a preceding paragraph. These spore-like bodies are seen

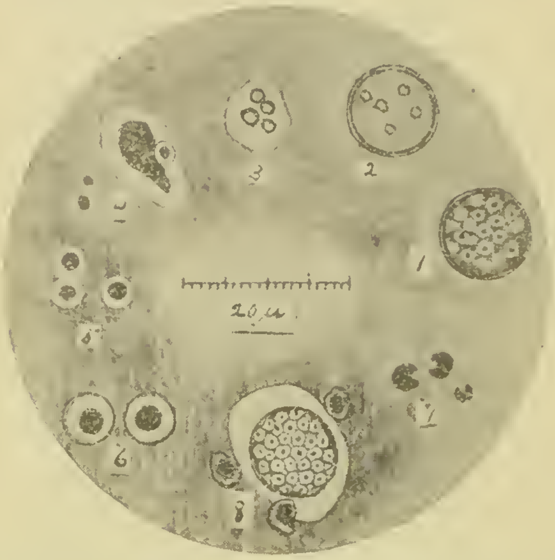


Fig. 3.—Sporulating forms and developing spores. 1 and 2. Adult forms containing spores. 3 and 4. Extracellular spore bodies; one at 4 is situated in protoplasm of tissue cell. 5 and 6. Developing spores. 7. Crescentic forms of developing spores. 8. Organism from guinea-pig's kidney, sporulating.

by careful focusing to be situated at the periphery and not at the center of the cells, the center being occupied by a large vacuole. They number from eight to twelve in a capsule. Exactly identical forms are seen as extracellular bodies, and other larger forms which have a crescentic shape and have evidently been formed by the development of these ring-like bodies, the chromatic substance increasing on one side and the hyaline center becoming eccentric, thus producing the appearance of a crescent. Further, there are found in these old capsules just described other small forms having a solid chromatic center surrounded by a hyaline area, and similar to the bodies appearing in the cells which we will now describe.

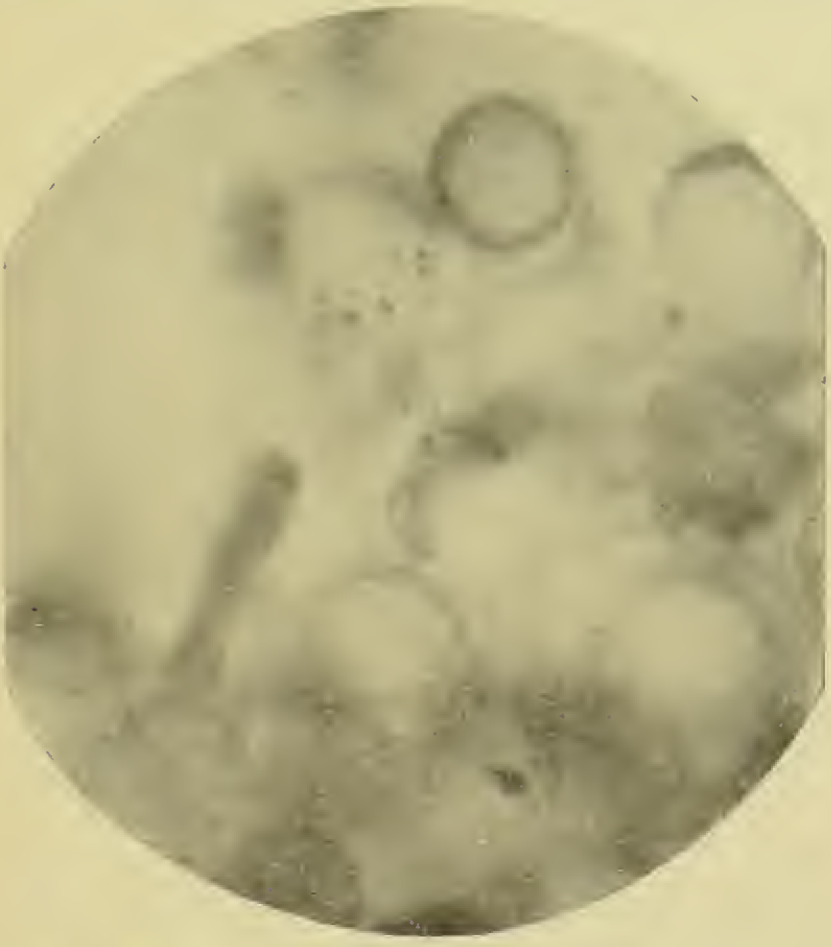


Fig. 4.—Showing spore-like bodies in disintegrating capsule (just above the center of the field).

There are certain cells which we have already mentioned which do not contain vacuoles, at least have no large central vacuole. In their later stages the protoplasm of these forms breaks up into small rounded hyaline bodies, many of which are seen to have a densely stained spherical center. Bodies exactly resembling these are seen outside the cells, and others, which are larger, one to three microns in diameter, and having about them the hyaline zone, but no distinct capsule as seen in the adult form. Some of these forms have been noted within tissue cells, and these tissue cells with their contained spore bodies are probably the beginning of the giant cells. As soon as these developing spores reach a size of about four or five microns a capsule is seen surrounding the clear zone. It was noticed that the parasites which are in the younger and smaller giant cells are mostly the smaller forms, while the older and larger giant cells contain older developmental forms of the parasites. It seems probable that the large rounded masses of parasites described in the pulmonary tissue are the result of further development of the giant cells.

The sporulating forms described here differ radically in the number of spore bodies formed within one capsule from the corresponding forms described by Ophüls in his systemic case, also from the forms pictured by Gilchrist.[12] They contain usually not more than twelve or fifteen, while Ophüls describes one hundred or more in each cell. However, we have noted in one of the guinea-pigs experimented on forms containing a very large number of spore-like bodies.

We have, then, two forms of cells producing spore-like bodies, one with a large central vacuole and one without, the bodies produced in these two forms being different in appearance, as already described. In no case have ruptured forms been observed in the tissues, the spores apparently being liberated by the disintegration of the parent organism. There is a possibility of confusing some of the extracellular developing spores with certain products of tissue cell degeneration.

---

[12] Gilchrist, T. C.: Blastomycetic Dermatitis in the Negro, Brit. Med. Jour., Oct. 25, 1902.

We have not absolutely observed the development of these spore-like bodies into adult organisms, but the appearance of the different forms which we have seen in the tissues leads us to believe that this is really the case.

THE BUDDING PROCESS.

The process of budding, as observed in the tissue sections, is almost entirely confined to the younger forms, those having deeply staining protoplasm and a wide, clear zone within the capsule. However, it is seen in other forms. A few cells are seen undergoing gemmation and apparently sporulation simultaneously. The different stages in the budding process are represented by a series of drawings in Figure 5.

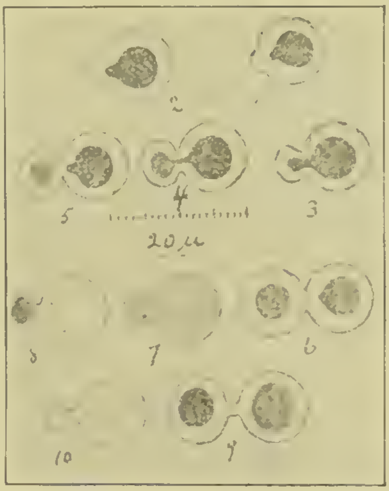


Fig. 5.—Budding forms. 1 to 6. Series showing progressive changes in process of gemmation. 7 to 10. Unusual forms. 8. Organism, budding and apparently sporulating simultaneously.

CHANGES IN THE BLOOD.

In the case of Busse,[3] where there was a fatal systemic infection, cultures of the parasite were made from the blood during life. In Gilchrist's case,[12] which he regarded as a beginning systemic invasion, examination of the blood by culture failed to reveal their presence. In the case under consideration, we have observed in the blood stream of vessels of the kidney (Fig. 6), also in other places, adult parasites mingled with the blood cells. On examination of sections of a postmortem clot from the heart practically all of the leucocytes were seen to contain large, brownish pigment granules of uniform size, from three to ten in a cell.

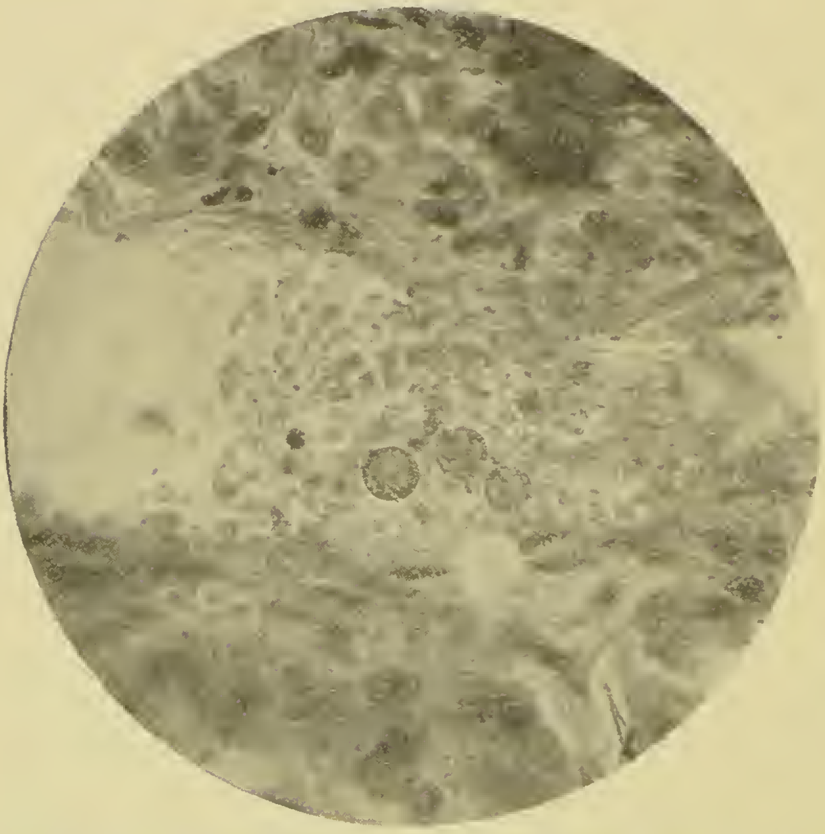


Fig. 6.—Three adult parasites seen in the blood stream of a vein of the kidney.

TEASED TISSUE IN HANGING-DROP CULTURE.

In the teased specimens of fresh tissue from the affected organs large numbers of blastomycetes were observed. They were not all of uniform size and structure. They varied from five to fifteen microns in diameter. The contents of the cell were often nuclear in appearance. Sometimes there were only granules present. Frequently the granular contents were lobular in appearance.

raspberry-like; again, they would assume a circular form about a large vacuole.

The cell wall is refractive and perfectly spherical. There is frequently one point where the capsule appears very thin, a point at which the protoplasm is often seen to protrude in the budding process. This is not always the point through which the growth takes place, for budding cells have been observed to produce mycelia from a point at sufficient distance from the point of attachment of the daughter cell to subtend an angle of twenty degrees. At the point where the mycelium appeared the capsule appeared to be perfectly firm.

Cell Development.—When hanging-drop cultures were first made, the cells varied considerably in size, but in a few days they had all reached a uniform size. As far as could be observed, no new budding processes took place after the cells had been placed in artificial media. Buds already existing grew to full-sized organisms. Some time later there appeared a few very large organisms (twenty to thirty microns in diameter) that changed their form from round to oblong. None of these large forms developed mycelia. In old mounts the cell contents of most of the organisms developed oil-like globules that varied from one to seven microns in diameter. In ten days some of them became so large that one globule occupied most of the cell. Some granule-like bodies manifested a very marked brownian movement. The formation of the fat-like globules seemed to be a process of degeneration, for the cells most exposed and those supplied with the poorest pabulum developed the largest globules.

Formation of Mycelia.—Thirty hours after hanging-drop cultures were made with bouillon for nutriment the cell started out small processes (Fig. 7). In the next twenty hours they grew sixty microns in length. The mycelia were homogeneous and possessed a very thin cell wall. Where the media was adequate, its growth seemed unlimited; but where there was but little media they grew slowly and developed a firmer wall. Protoplasmic granules and pinkish vacuoles formed in the processes. Soon these granules became smaller and more dense. Then they manifested a very active brownian movement. After the mycelia were several days old, there appeared a subdivision of the mycelia into cells or segments of varying length (ten to one hundred microns).

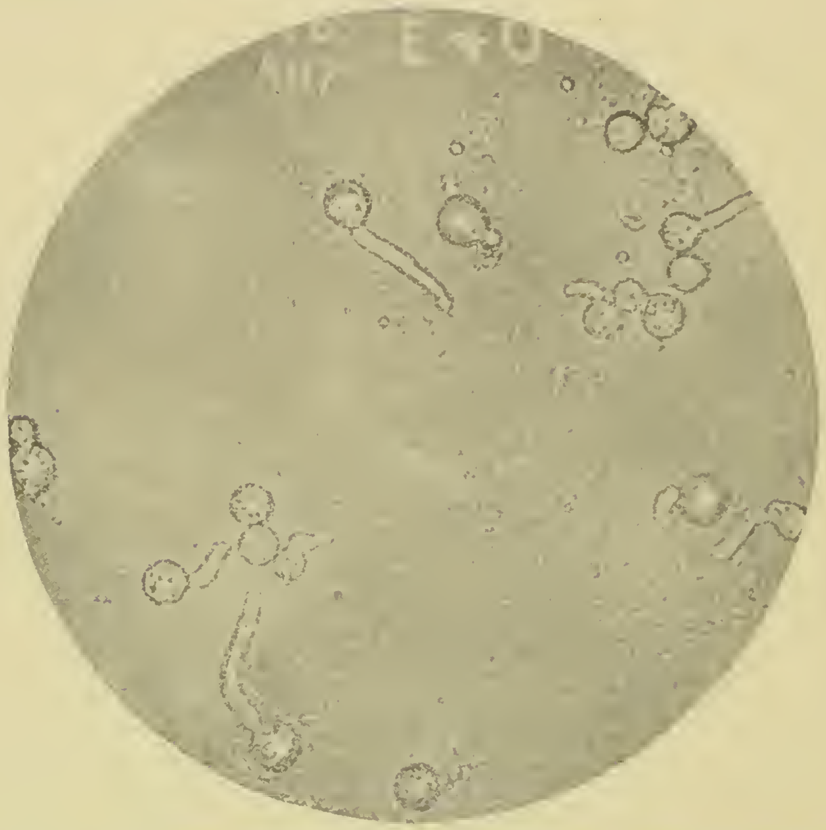


Fig. 7.—Blastomycetes. Teased cells from spleen beginning development in artificial media.

These segments near the focus of growth continued to develop, assuming a spherical form.

After a hanging-drop culture in glycerin bouillon had developed for about a month there appeared an end cell that budded. In a few days there were four cells. These, as in several other places, developed until there were a dozen or more in a cluster.

Fortunately, one hanging-drop culture had but six microörganisms present, thus giving excellent opportunity to observe them individually. One of the budding forms started a mycelium. The process originated from a point near the attachment of the daughter cell. Shortly after the mycelia divide into segments, many of them sending out processes (Fig. 8). There were no more than one process from a given segment. The granules that formed in the mycelia showed a more marked brownian movement than particles in the surrounding fluid. It was as marked as the motility of the pigment in the malarial parasite. This movement lasted for more than two months. It was observed also in the mother cell. As the plant became older there appeared an extra development of some of the individual cells in the thread. They took on a spherical form, and produced a protoplasm similar to the protoplasm of the cells in the teased specimen.

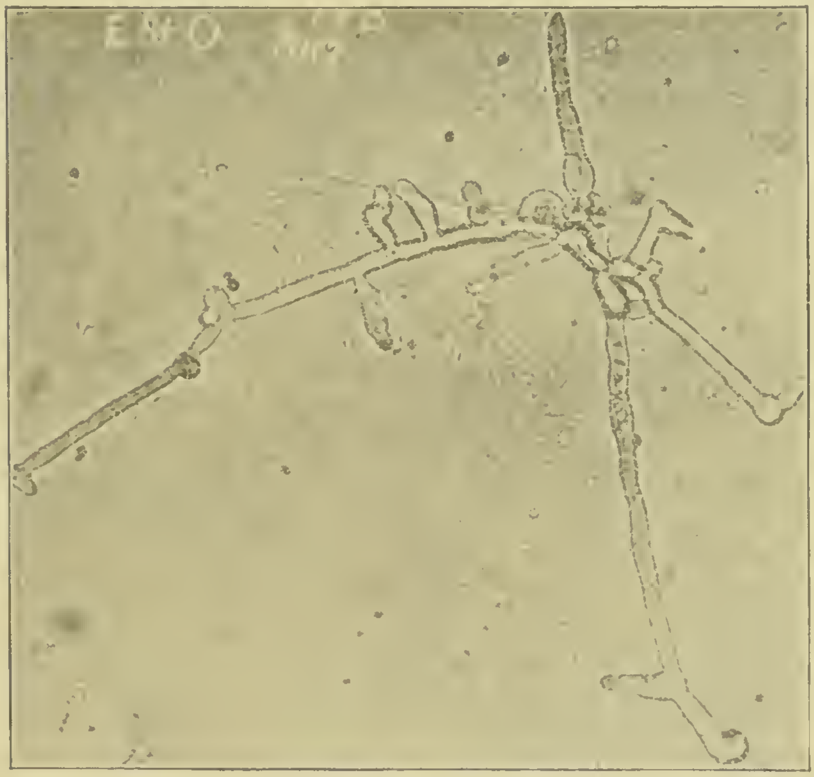


Fig. 8.—Blastomycetes. Dividing cell after ten days' growth in hanging-drop culture.

CULTURAL CHARACTERISTICS.

Petri Dish.—Six to nine days elapsed after a culture was made before any macroscopic signs of development appeared. Then a white area composed of radiating threads might be seen about the center of growth. If the cultures are observed with a microscope, these threads may be seen a few days earlier. One or more mycelia may be seen growing from a point as early as the third day. These soon subdivide, others are given off nearer its point of origin; these grow out in radiating lines, subdividing as they grow. The growth may be very rapid, the mycelia increasing two millimeters in length in a day. The rapidity of the growth did not seem to depend on the temperature so much as it did on the amount of moisture in the atmosphere. The most rapid growth was manifested when the Petri dishes were kept so there was considerable moisture condensed on the inner surface of the covers. In the Petri dish the most rapid growth was manifested in gelatin. It is interesting to note that in all media for some days no aërial hyphæ were produced. Instead, the growth spread beneath the surface in all directions. Later, however, the white aërial hyphæ appeared near the center of the growth.

Bouillon Culture.—Blastomycetes developed in plain, saccharin, glucose, lactose and glycerin bouillon. It is the most rapid and luxuriant in the glycerin bouillon. It grows most readily and rapidly on the surface and clings to the side of the tube very closely. It forms a mycelial growth on the surface of the bouillon so firm that it will prevent the bouillon flowing when the tube is inverted. If the tube is shaken a little after the growth develops, it is forced away from its position on the side and has the appearance of cotton. It never has developed the powder-puff appearance in bouillon. It is quite perfect in agar-agar, however. The teased membrane from the surface of the bouillon showed numerous conidia, three to six microns in diameter. There were also large conidia invariably filled with spore-like bodies. A little pressure between cover slips would liberate the contents of these bodies. Then all the appearances of the cells from teased tissues were observed. These large forms varied in size from seven to fifteen microns. Their arrangement in the teased materials suggested that they grew individually rather than in clusters of conidia.

Agar-Agar.—As has been mentioned, the early growth is quite completely beneath the surface. The growth is silvery white and forms a powder-puff-appearing hemisphere. It sometimes remains entirely beneath the surface and does not wrinkle. Again, it may wrinkle the surface. Sometimes eminences are thus formed from which beard-like tufts of aërial hyphæ are given off. As the culture advances in age it becomes slightly brown. The illustration will show the forms of growth as they appeared under the microscope. Conidia filled with spore-like bodies were also observed. The hyphæ varied much in diameter. There were some very fine forms measuring less than one micron.

Gelatin.—The gelatin plate grew very rapidly and did not wrinkle. No liquefaction was observed. The stab culture grew most rapidly at the surface. No liquefaction was observed in stab culture until after a month, when it was noted that the entire gelatin had gradually liquefied. At the end of three months it is perfectly fluid.

Litmus Milk.—The growth is rapid and abundant. The media changed to a deeper blue.

Potato.—The growth was as rapid as on plain agar. It was white and appeared like froth as the potato dried.

Loeffler's Blood Serum.—The growth was abundant, and did not seem to be more rapid than on glycerin agar. The color was not any different than what might be imparted by the media. There was no liquefaction.

Motility.—The motility of the protoplasmic granules was observed, but there was no motility of the entire microörganism.

Oxygen Requirements.—The cultures grown anaërobically by the Novy method showed no signs of growth in a month; but when removed from the hydrogen developed growth in seven days. A microscopic examination of material from the surface of the culture when taken from the jar showed no growth and no unusual forms.

Gas.—Although growth took place quite readily in the fermentation tube, no gas was produced, though grown in lactose, glucose and saccharose media.

By-Products.—No alcohol was developed in bouillon above mentioned. No carbon dioxid was produced in quantities that could be detected. There was no nitrite or indol produced.

Destruction by Heat.—Growths in which there were aërial hyphæ grew readily after being exposed to 100 degrees C. for five minutes; while, if the hyphæ were submerged in bouillon before submitting to the heat, they were destroyed in less than five minutes at 54 degrees, centigrade.

Destruction by Antiseptics.—The microörganism is destroyed when exposed as follows: Five per cent. carbolic acid, for one minute; 2 per cent. commercial formalin, one minute; 1/1,000 bichlorid, for one minute. When exposed to 2 per cent. hydrochloric acid, specific gravity 1,320, for fifteen minutes, it not only was not destroyed, but it seemed to grow more rapidly.

Animal Experiments.—Of five guinea-pigs that were successfully inoculated, four developed ulcers at the point of inoculation. One developed simply a nodule. The ulcers were oblong, having the long axis parallel with the long axis of the body. In the center of a typical ulcer there is a dry, bloody scab. If this is raised it bleeds readily, while there may also be seen many pin-head-size gray foci. They suggest the miliary pustules characteristic of the human skin lesion. Around the central portion is a raised slightly indurated area from which the hair has fallen. The third day after inoculation one animal developed a subcutaneous abscess from which a bloody fluid was evacuated in which blastomycetes were observed. Two weeks after inoculation a ridge was noticed from the ulcer along the sternum to the clavicle, suggesting an enlarged lymphatic. The animals died a month after inoculation, all within a few days of each other. Although an epidemic was suspected it could not be proven bacteriologically, as blastomycetes were found near the seat of inoculation, while from the liver and spleen a pure culture of blastomycetes was grown in one instance. Cultures taken from the internal organs of the other animals did not develop any growth. However, had a larger number of cultures been made undoubtedly a positive result would have been more often obtained, for two-thirds of the successful cultures in the one case were negative. The lesions observed were numerous. Infarcts appeared in the lungs, kidneys, spleen, and in one case seven small, round hemorrhagic infarcts were observed in the stomach wall. Pin-point foci were seen in the liver and spleen. An ulcer was noted in the upper intestine. There was also quite an inflammatory condition in the axilla and groin, but no general glandular enlargement could be seen. One guinea-pig inoculated with material from agar-agar died in two months and manifested similar lesions to the above. Two rabbits were inoculated with teased tissue. Both lost in flesh, one more rapidly than the other. One is living; the other was killed five months later. No lesions were observed except numerous subcapsular scars in the kidneys. The microscopic study proved that they were a healing infarct. Two mice were inoculated with a culture after four months of artificial cultivation. They are alive after three weeks.

The microscopic study of the organs of the animals unfortunately has not been completed; nevertheless, quite a complete study was made of those of the guinea-pig dying of systemic infection. The same kind of lesions were noted as in the human. One observation is especially worthy of mention, namely, many large cells, apparently sporulating forms, as mentioned by Gilchrist,[12] were observed in the kidney sections.

There has also been a case of accidental infection following this case. The microörganism has been isolated in pure culture. It has also been observed in sections.

Experiments were undertaken to determine the effect of the *x*-ray on cultures of blastomycetes. They were exposed in Petri dishes with covers of oiled paper for periods from ten to thirty minutes in length every third day for two weeks. No visible effect was produced.

An ordinary sixteen-plate static machine was used with an *x*-ray tube of low tension. The distance of the tube from the cultures was two inches.

Cultures prepared in a similar manner were exposed to the influence of the light of an actinic ray apparatus. In these specimens, the growth of the organisms entirely ceased. However, a certain amount of heat was developed in the exposures, and it is impossible to determine whether the effect was due to the heat or to the influence of the actinic ray.

During these experiments, a very interesting observation was made. The paper covers of the Petri dishes were oiled, some with paraffin, others with cedar oil, to make them more transparent. In the case of those which were exposed to the *x*-ray, those cultures which were under the paraffin paper grew with their usual activity, while the growth of those under paper prepared with cedar oil was absolutely inhibited, and by culture experiments from those plates it was determined that the life of the parasites was destroyed. In a later experiment in which cultures were employed which had been growing for nine days, and in which the colonies had reached a considerable size, their further growth was entirely prevented by the cedar oil paper, while they continued to develop at a rapid rate in the control plate. In this case the cultures were exposed simply to the influence of the cedar oil, no other agents being used which might effect their growth. Subcultures from these plates made after an exposure of seven days to the effect of the cedar oil paper showed that the organisms were not yet destroyed, although absolutely inhibited. This observation may possibly prove to be of some value in the treatment of blastomycetic infections.

SUMMARY.

1. This case is one of systemic blastomycetic infection and belongs to a class of which but a very few instances have been reported.

2. Parasites were demonstrated in the blood postmortem and dissemination evidently took place through this medium.

3. The lymph glands are remarkably free from infection.

4. In the lesions the parasites were found in immense numbers, and the inflammatory reaction in the tissues were of a remarkably slight degree.

5. The leucocytes of the blood and certain tissue cells contained large quantities of round pigment granules.

6. Parasites grow in the tissue only by budding, the forms appearing from five to fifteen microns in diameter; in artificial culture by segmented mycelia, lateral conidia, and in very old cultures a few budding forms.

7. There is a definite order of development of the parasite in the tissue, the younger forms having a densely staining protoplasm undergoing active cell division by gemmation; the older forms not deeply staining and not actively dividing, and containing spore-like bodies.

8. From the findings in the tissue it seems evident that sporulation occurs, five to fifteen spores developing in each cell where they are seen.

9. Organisms derived from teased tissues have been observed in hanging drop to produce mycelia within a few hours after they were removed from the tissue.

10. The effect of exposure to the x-rays was negative.

11. The effect of the actinic ray is doubtful because the element of heat was not eliminated.

12. The cultures covered with cedar oil paper died within one month. Those exposed for one week were completely inhibited from growth, but were not dead.

13. The organism fulfills the laws of Koch, guinea-pigs being more susceptible than rabbits.

14. The organism grows readily on all forms of artificial media used.

15. In gelatin liquefaction was produced after one month.

UNCINARIASIS IN THE SOUTH.

FURTHER OBSERVATIONS.

CLAUDE A. SMITH, M.D.
Pathologist to Grady Hospital; Demonstrator of Pathology and
Bacteriology, Atlanta College of Physicians and
Surgeons; Professor of Pathology and Bacteriology, Southern Dental College.
ATLANTA, GA.

Since presenting the paper before this Section at the meeting in Saratoga last year, in which I reported three cases of ankylostomiasis, or uncinariasis, the first case being found postmortem, in December, 1901, and the other two being mild cases found among the negro convicts working in the brickyards near Atlanta, I have found this disease to be exceedingly common from the Carolinas to Texas. I make this statement as a result of examinations of medical students at the Atlanta College of Physicians and Surgeons, at the Southern Dental College, patients sent to Atlanta from the adjoining states and a systematic examination of all the patients in the Grady Hospital for the past year. However, very few cases have appeared at the Grady Hospital for the reason that all the patients in the public wards must be residents of Atlanta, and, as this is a disease of the country and not of the city, we would not, therefore, expect to find many in the hospital. Since the postmortem on the case reported last year, I have made fifty postmortem examinations at the hospital, and among these have had only one case of uncinariasis.

This disease is found in the mountains as well as in the lowlands, but is more common the farther south you go, as the conditions for the production and development of the larvæ are more favorable. The disease is very common in regions where the chances of contamination of the drinking water with surface drainage is very slight.

The disease may occur at any age, but is more commonly found in children. The cases seen by me range from three years to over fifty years of age. It is more common in males than females, and is usually found among the children of the lower classes, but I have seen several cases among the better class. It appears to be more frequent among the whites than the negroes. It is a disease of the country, and the possibility of its presence should be considered in all patients who give a history of having resided in the country or small villages within seven or eight years. It prevails where unsanitary conditions abound.

The eggs of the parasite are passed in the feces of persons affected with the disease, and these feces, being deposited about on the earth, furnish the original source of infection. The life history of the parasite found in the dog and the one found in man is very similar, but I have not been able to infect one from the other.

I have found the eggs in the stools of a dog, and a careful postmortem examination showed only three of the worms in the intestine of the dog. This shows that no matter how small the number of worms may be, it is possible to find the eggs in the feces. Practically, the same thing applies to the parasite found in the human intestine, as one case disclosed only seven worms postmortem. It is possible for one experienced in making these examinations to give a fair idea of the number of worms in the intestine from the number of eggs appearing in the stools. They can be estimated with a greater degree of accuracy in this way than by the symptoms of the patient, as a comparatively small number in one person will produce severer symptoms than a larger number in another person.

A live uncinaria removed from a dog under chloroform was seen by me to discharge 22 eggs in one minute, and while this was taking place there was no appreciable diminution in the quantity of eggs contained in the uterus of the worm. This gives us some idea of the great number of eggs which may be thrown off by one worm.

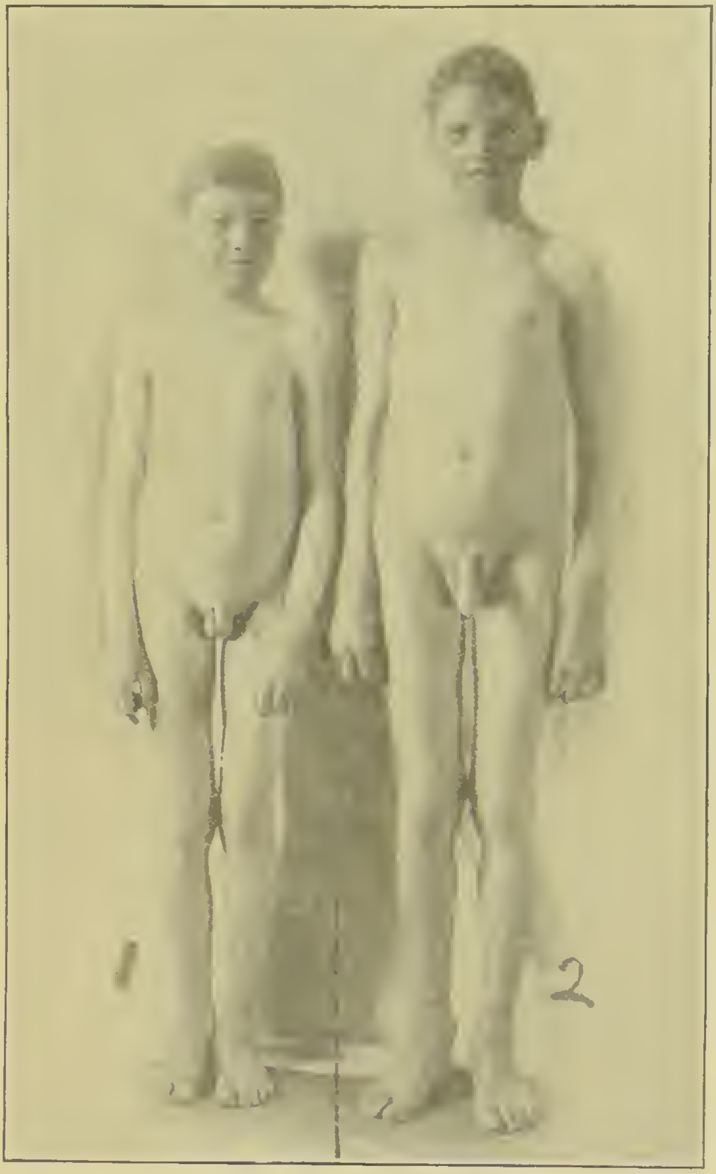
As a rule, the eggs do not hatch while in the intestines. I have found the larvæ hatched out in only two specimens of feces. Usually, it is necessary for the eggs to become mixed with earth before they will begin to hatch; that is, they seem to need air. The eggs can be hatched without any difficulty if the feces containing the eggs are mixed with sufficient earth or sand to destroy the odor of the feces. They will hatch in from twelve to twenty-four hours, or longer, depending on the temperature and moisture; too much moisture inhibiting their development.

They are destroyed by freezing, as also by drying, but they must be thoroughly dry, the least bit of moisture preserving them. Feces which are perfectly dry on the outside will be found to be moist in the interior and the eggs there still preserving their vitality. In warm weather, if the eggs are kept in moist feces, I have been unable to hatch any of them after two weeks. In hatching, I have observed the larva emerge tail first from the egg.

For the first day or so the larva is rather sluggish, but as the first sheath appears it becomes more energetic and is extremely lively at times. If in water alone it wiggles at a lively rate, but does not make much headway, but if imbedded in earth or sand, where it can obtain a foothold, by a sinuous motion it darts through sand at a lively rate. These periods of activity are of variable duration. The larva will move quite lively for from a few minutes to half an hour or more, and then it will straighten out and lie perfectly still for a corresponding length of time.

Freezing destroys the larvæ, as will also drying. However, it should be remembered that soil which to the naked eye appears perfectly dry will, on examination with the microscope, be found to contain a small amount of moisture, and such an amount as is sufficient to preserve the vitality of the larvæ. But, if they do become thoroughly dried, if only for a moment, they can not be revived. Knowledge of the conditions under which these larvæ exist are of great value in determining when and how the disease may be contracted. When we remember that it freezes every winter throughout the South down through the northern part of Florida, we can readily see that the disease could not be contracted in the winter; also, as drying destroys the larvæ, their existence is a very precarious one. However, during the warm summer months, when there is a rainy spell, the ideal conditions prevail for the development of the larvæ, and so this is the time at which we would be most likely to encounter them.

The next point which concerns us is, how do they reach the intestinal canal? It was not suspected until the last few years that it could reach the intestines other than through the mouth, and especially as moisture is necessary for the existence of the parasite it was supposed to gain entrance principally through drinking water. However, since Looss has demonstrated that the larvæ may pass through the skin, and Bentley has attributed the pani-ghao, or ground itch, to the larvæ, it has opened up new avenues for investigation. At first consideration of this view I was loath to believe that the parasite could gain entrance by passage through the skin, as it appeared to me more probable that it made entrance through drinking water. But after a careful observation and investigation of the habits of the larvæ and of the disease itself as it exists, I was forced to the opinion that in the great majority of cases they gain entrance through the skin of the feet, and that the true ground itch is simply the manifestation of this passage. There is no doubt that some cases may be produced through drinking water, but my observations of the development of the larvæ and the conditions surrounding the disease have led me to believe that this is



Case 1.—17 years of age. Case 2.—15 years of age.

These two are brothers. Examination of stools showed a great number of eggs of uncinaria in stools of No. 1, and comparatively few in stools of No. 2. This illustrates the lack of development in the extreme type of uncinariasis. No. 1 is two years older than No. 2, yet presented the appearance of a boy of 12 years, with no development of sexual organs. No. 1 is unable to do any work, While No. 2 is apparently as vigorous as other boys.

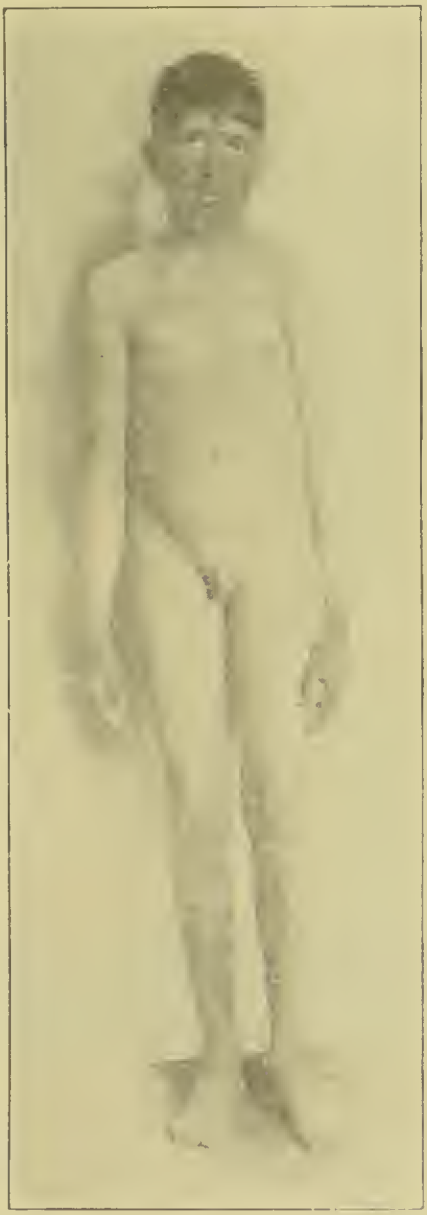
the exception and not the rule. That infection could take place through dirt on the hands and then taken into the mouth I am also inclined to believe is the exception, even more so than infection through drinking water, for it is likely that the larvæ would become destroyed by drying before they would be taken into the mouth.

Ground itch is the most common disease in the South, and the majority of cases are never carried to the physician, but are treated with home remedies. It appears in the summer and always as a result of going barefoot in wet weather. In many sections in the South it is thought to be the result of being poisoned by the dew, but it is always contracted at the time when the ground is damp, which is the condition most favorable to the development of the larvæ of the uncinaria. In some districts they take great pains to try to keep the children indoors during rainy weather, and especially when it rains several days, so as to prevent them from having this ground itch. One patient told me that he was fond of wading in ditches after a rain, and he was sure that the foam which collected along the sides of the ditches contained the "poison," as he always had an attack from wading in that foam.

The first symptom of ground itch is an itching between the toes, which begins after going barefoot in the mud. It may appear at one place between two toes, or it may appear between all of the toes, and also under them, and in some cases may extend up some distance on the foot. This itching increases and the skin becomes very red, and finally small vesicles are formed. The itching continues and these vesicles are usually ruptured, leaving a raw weeping surface. The itching is generally excruciating, and the condition may last two, three, four or more weeks.

The following is some of the evidence in favor of the ground itch being the method of entrance into the human body of the larvæ:

Every person who has had true ground itch within seven or eight years will have the eggs of the parasite in their stools. This time limit is not positive as yet, but the evidence points strongly to a limit of about seven years.

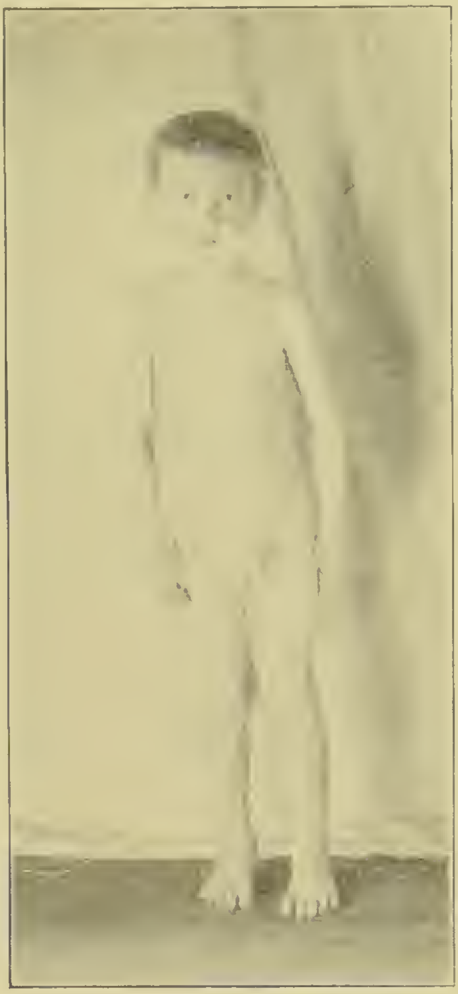


Case 3.—White; male; age 17. Skin resembles yellow parchment; mucous membranes blanched; appetite poor; sleeps fairly well; has severe griping of bowels at times; badly constipated. Red corpuscles, 1,672,000; hemoglobin, 22 per cent. Notice lack of development of sexual organs. Has had "ground-itch" so many times that can not recall any year that he did not have it. Stools contain eggs of uncinaria in great numbers. Barely able to get about, and unable to do any work.

You can form a fair estimate of the number of eggs that you will find in the stools by taking a careful history of the severity and extent of the number of attacks of ground itch. For example, if a patient gives a history of having had a number of attacks of ground itch which involved all of the toes and possibly a portion of the feet, you will find a great number of eggs in the stools of that patient. In the last postmortem in which I found the uncinaria in the intestines, I saw the patient just two days before her death, and in getting her history learned that she had had an attack of ground itch about four or five years previously, but she informed me that she did not have it very bad, as it existed only in one place between two toes. A careful search at the postmortem examination disclosed only seven of the worms. I have seen only two cases of the disease which did not give a history of having had ground itch within seven years. They were two dental students who lived at the same place in Florida, and they were both sure that they had not had ground itch for fourteen or fifteen years. However, their drinking water was obtained from wells only three or four feet deep and which overflowed every time it rained. These were probably infected through drinking water, but in both cases the infection was very slight, as it required careful search to find the eggs in the stools, as they were so very few in number.

Many of the cases of the disease were suspected and located only on finding a history of having had ground itch within seven years. One was a medical student from the mountains of South Carolina, who presented a picture of perfect health, with a ruddy complexion, and who did not suspect that he had uncinariasis until he overheard a conversation about the relation of ground itch to the disease. He then came to me and told me that he had had a severe attack of ground itch about five or six years before, and on examination of his stools I found numerous eggs of the uncinaria. Examination of his blood showed: red corpuscles, 4,120,-

000, and hemoglobin, 95 per cent. After two doses of thymol of one gram each, eighteen uncinaria were found in his stools and no eggs were found a week later. It usually requires several attacks of ground itch, extending over a period of several summers, for sufficient numbers of the larvæ to get into the system to produce the extreme type of the disease.



Case 4.—White; male; age 7. Skin yellowish-white; mucous membranes blanched; appetite poor and perverted; bowels constipated; shortness of breath; loud hemic murmur; can not walk over 200 yards at a time; headache and vomiting every morning; stools contain an abundance of eggs of uncinaria. Red corpuscles, 1,208,000; hemoglobin, 10 per cent. Has had "ground-itch" every year since able to walk. Has had whooping cough, but no other sickness.

A careful examination was made of all the members of a family of eight who had lived under the same conditions, drinking the same water, etc., and this showed that those who had been keeping the feet protected for over eight years by wearing shoes, and who had not had ground itch during that time, did not have the eggs in their stools, while all who had had ground itch within that time had the eggs in quantities in direct proportion to the number and severity of the attacks of ground itch.

You may take the history of some of the cases which have at one time been in the extreme stage, and you will find that they had attacks of ground itch year after year, or probably skipping a year now and then, and they would get worse from year to year until they had had attacks covering a period of seven years or more, and probably they were old enough by that time to begin wearing shoes in the summer time, and, therefore, those parasites which first gained entrance into the body would have passed through their allotted period of existence and would die out, and by the patient wearing shoes, additional larvæ would fail to get into the body, and as each following year more and more of the uncinaria would die out, the patient will give a history of gradual improvement, and his body will begin to take on a vigorous development. There is no difficulty in finding plenty of these cases which give a history of having once been extremely pale and anemic, but have "outgrown" it. The disease gradually disappears after they stop going barefoot.

The number of the uncinaria in the intestines varies from a few to several hundred. The number is nearly always in direct proportion to the number and severity of attacks of ground itch. A few of the uncinaria may produce no apparent effect on the patient, but it no doubt renders the patient more susceptible to infection as a result of the interference with the nutrition. Severe infections produce various grades of anemia. The blood counts show all stages; some being so severe as to produce dizziness, hemic murmurs and the weakness which accompanies such conditions. These extreme cases are usually emaciated, but the emaciation may not be apparent at first on account of edema. In the extreme cases the skin is of a yellowish-white parchment color, and over the exposed portions of the body, as the cheeks and hands, it appears to be much thickened. The mucous membrane also presents a yellowish-white blanched appearance, and examination of the blood often shows the red corpuscles as low as 1,100,000, and the hemoglobin down to 10 and 15 per cent. If this severe condition is reached about the time of puberty, the sexual development does not take place, and it is not uncommon to see boys 17 and 18 years of age who are dwarfed and whose genital organs have the same appearance as those of a boy about 10 years of age. Also, you will find girls 18 years of age in whom there has never been any effort at menstruation, and who present no evidence of development into womanhood. We must remember that these are the extreme cases. They are the ones which give a history of numerous and severe attacks of ground itch, usually having it for a number of years, and members of the same family who are living under exactly the same conditions, but who have not had so many, nor such severe, attacks of ground itch will have only a small number of parasites in their intestines, and practically no interference with their development.

It is a most pitiable sight to see these severe cases in bright children who are unable to walk 200 yards without being almost completely exhausted and who have to sit down and rest before they can go further. They are unable to play the games with other children, but must drag out their lives sitting and lying around, watching the other children in their games and yearning for the strength to join in with them. Sometimes they succumb to additional infection of the uncinaria, or to attacks of other diseases.

In their earnest desire to be cured and become strong like other children, they are willing to undergo any treatment which will offer any chance of doing them good, and often you will find that they have made the rounds of all physicians in their district, but to no avail. I recall the case of one poor boy who was barely able to drag himself about, and on being told that there was a chance of something being done for him, he arose early in the morning only to find that the rain was pouring in torrents, but, nothing daunted, he dragged himself all alone three miles through the pouring rain to the physician's office, drenched to the skin and shivering with cold, but willing and anxious to begin at once with any treatment that offered any chance of doing him good. That was only three weeks ago, and since then his improvement has been remarkable, as he is now at work again on the farm.

Every country practitioner in the South has more or less of these cases of anemia in his practice, and sometimes they will improve slightly with prescriptions of iron, arsenic, etc., but with no permanent results.

The poor farmers throughout the country who have a house full of children to support are dependent to a great extent on the assistance of these children to make sufficient for their maintenance, and when the children are affected with this disease and are unable to assist him to any extent, but rather instead are a burden to him to pay their physician's bills and supply medicine—these are the ones who often seek the cotton mill, where most of the children, although dwarfed and stunted and incapable of severe exertion, yet have sufficient strength to sit at a loom and do light work about the mills. While it is deplorable that child labor is not better controlled, and, while I believe in giving the devil his dues, yet we should, at the same time, be just, for no doubt many of the cases of children whose lives are supposed to be blighted in the cotton mills, were blighted before they went there, and the confinement and tedious work is but assisting in the work of destruction already begun.

We read our statistics of the destruction wrought by the dreaded tuberculosis and pneumonia, etc., but we have here a disease which is literally sapping the life-blood of the South. But, unlike tuberculosis and pneumonia, etc., we have for this terrible disease an easy means of diagnosis, and a cure which is simple and certain. All that is necessary is for the physicians throughout the country to become familiar with the diagnosis and treatment.

Before treatment is instituted, a positive diagnosis can only be made by the examination of the stools for the eggs, and one experienced in examining these stools with the microscope can get a better idea of the number of parasites in the intestines than from the symptoms of the patient.

The treatment is very simple, but to be thoroughly effective certain precautions should be observed. Two doses of thymol finely powdered of one or two grams each are to be given about two hours apart. The first dose should be preceded several hours by a dose of some purgative, and followed by the same. One very important point is that no food must be taken into the stomach from the time of the first dose of the purgative until after the second is taken. The plan is as follows: A large dose of salts is given at night and the next morning at 8 o'clock two grams of *finely powdered* thymol is given, and two hours later a second dose of two grams, and two hours after this a large dose of salts is given. I lay stress on having the thymol finely powdered and no food being taken into the stomach between the administration of the purgatives. In some instances this treatment is not thoroughly effective, and a microscopic examination of the stools should always be made about a week later, and if eggs are still present, the treatment should be repeated.

In the postmortem examinations of the human intestines containing the uncinaria, I have noticed that the parasite is not so firmly attached to the intestinal mucous membrane, and also that it does not seem to lacerate the mucous membrane, or leave the white central spot with the hemorrhagic area surrounding it, as described of the old world parasite, and also of the parasite in the dog. We can readily understand this when we bear in mind the structure of the oral cavity of the uncinaria, as given by Dr. Stiles, showing that it does not have the little hooklets which are found in the old world parasite and the dog in this country, and, therefore, does not become so firmly attached or so severely lacerate the mucous membrane.

The prophylaxis of this disease is very simple. It is not necessary to boil the water for drinking purposes, unless the water has been contaminated by surface drainage after a rain. If every person will wear shoes which thoroughly protect the feet in rainy weather or in damp places, there is very little chance of infection.

To determine whether the parasite which infects the dog in my section would exist in the human body, I administered successive doses of the larvæ of this parasite to a negro boy 19 years of age (of course, with his consent), beginning the first dose July 11, 1902, when the larvæ were four days old, and continuing about every two weeks until October 14, using larvæ from the original culture made July 7. The patient disappeared October 14, but examinations of stools two days before that were negative.

In making these investigations, I was much indebted to Dr. S. H. Green of Bolton, Ga., and Dr. C. D. Redding of Warthen, Ga.; also to Drs. J. A. Randall, W. E. Persons, C. D. Jeffries, O. T. White and W. A. Selman, of the resident staff of Grady Hospital.

DISCUSSION.

Dr. H. B. Ward, Lincoln, Neb.—Dr. Smith has gone further than any other investigator with reference to the life history. It is of the utmost importance that the method of introduction into the body should be known, as well as the interval between the various stages of development. Dr. Smith has investigated the relation between ankylostomiasis and ground itch so thoroughly as to leave little doubt as to their probable connection. I think the probability is very strong indeed. One of the latest investigators records the fact recently in one of the German journals that he has succeeded in infecting the skin with the larvæ. The larvæ were placed on a member which was about to be amputated. When the skin was sectioned after the amputation the larvæ were found to be penetrating the skin along the line of the hair follicles, and they could be made out in the sections. Some had gone in as far as the subdermal tissue. I think that is the first instance where the entrance of the larvæ has been thoroughly established.

Another point deserves brief mention. The experiments of Looss on dogs shows conclusively to my mind that the infection can not be contracted through drinking water. Where the dogs were fed on infected water the larvæ passed through the canal, except a few which bored into the wall of the esophagus and went down into the tissue, where he got the three stages of development. Those which traversed the canal did not attain the adult condition, but those which got into the tissues attained at least the later larval stage.

I presume Dr. Smith has already thought of it, but it would seem to me that in the region where ground itch prevails he might succeed in some postmortem in getting a portion of the tissue from one who had been recently infected with ground itch, and sections made from this would throw light on the subject.

Dr. Claude A. Smith, Atlanta, Ga.—I recognize the fact that the results so far are somewhat incomplete, and that we have not been able yet to obtain positive proof as to the transmission of the disease. Experiments are being still carried on, from which we hope to obtain more satisfactory results. Until then it can not be stated positively that the infection does get into the system through the feet, but from the evidence of cases I have seen I feel positive that this is so.

As to the question of postmortem of subjects who have had ground itch, it must be remembered that these cases are nearly all in the country, and you know how difficult it is to get permission to hold a postmortem in the country, especially in the case of children. They even object sometimes to examination of the stools.

I hope in the near future to be able to present the proof of the transmission of the disease.

THE CAPACITY OF A HUMAN MUSCLE FOR WORK.

JESSE GEORGE HOLMES, B.S.
From the Physiologic Laboratory of Northwestern University Medical School.
CHICAGO.

HISTORICAL REVIEW.

Each year adds its share to the work that is being done by the different investigators in the study of muscular contractions, neuromuscular fatigue and the ability of a muscle to do work. To Mosso[1] must be given the credit of first making investigations with the human muscle. The instrument used by him in his work consisted in a weight and pulley. The muscular power obtained he expressed as weight multiplied by the distance through which it was raised. Maggiora,[2] Lombard,[3] Treves,[4] Cleghorn and Stewart,[5] Storey[6] and others continued investigations, introducing various modifications into the technic, thereby obtaining results of considerable value and interest.

Thus the original idea and the one followed more or less closely since has been to have the muscle raise and lower a weight successively through a given distance. It was found that a muscle can raise the weight at a regular rate until, as fatigue sets in, the height of the contraction becomes less and the movements become slower and more difficult. The amount which a muscle can do depends on the muscle and the technic used, the rapidity with which it contracts and the weight it has to lift. Among the objections that soon became evident are the following: (1) That the muscle after a short time becomes so fatigued that it can no longer lift the given weight. It can still exert a considerable amount of force, and if a lighter weight be used it can lift it. (2) It is found that only isotonic contractions are possible in the use of the weight ergograph, and that the muscle is under a continuous tension. (3) The greatest tension of the muscle is that required to overcome the inertia of the weight in starting it.

---

[1] Mosso: Ueber die Gesetze der Ermudung. Archives für Physiologie, 1890, p. 89.

[2] Maggiora: Ueber die Gesetze der Ermudung, Archives für Physiologie, 1890, p. 191.

[3] Lombard: Some of the Influences Which Effect the Power of Voluntary Muscular Contraction, Jour. of Physiol., 1892, xiii, p. 1.

[4] Treves: Sur les lois du travail musculaire, Archiv ital. de Biol., 1898, xxx, p. 1.

[5] Cleghorn and Stewart: Inhibition Time of a Voluntary Muscular Contraction, Amer. Jour. of Physiol., 1901, v.

[6] Storey: The Influence of Fatigue on the Contraction of Human Muscle, Amer. Jour. of Physiol., 1903, viii, p. 355.

Others, thinking that with the use of the weight the muscle does not work to the greatest advantage, employed the spring. Cattell,[7] Binet and Vaschide,[8] Franz,[9] Hough,[10] Fick[11] and others have used this form quite extensively, but it has not replaced the use of the weight entirely. The advantages of the spring over the weight are the following: (1) The slightest movement made by the muscle can be recorded, whether it is of the isotonic or isometric form. (2) An interval of rest is allowed the muscle between the periods of relaxation and contraction. (3) The inertia is less pronounced. On the contrary, however, Franz[12] says that most of the objections which apply to the weight will also apply to the use of the spring. Thus it may be seen that the introduction of the isometric contraction, a condition not possible with the weight, has added interest to the study of action of a muscle.

---

[7] Cattell: Science, N. S., 1897, v, p. 909.

[8] Binet and Vaschide: Annee psychologique, 1898, iv, pp. 245. 253. 303.

[9] Franz: Methods of Estimating the Force of Voluntary Contractions and on Fatigue, Amer. Jour. of Physiol., 1901, iv. p. 348.

[10] Hough: Ergographic Studies in Neuro-Muscular Fatigue, Amer. Jour. of Physiol., 1901, v, p. 240.

[11] Fick: Pfluger's Archiv für Physiologie, vol. xli, p. 176.

[12] Cf. p. 353.

GENERAL CRITIQUE.

In answer to the objections to the weight or spring ergograph, it has been mentioned that most of them are objections either to the mechanical construction which might easily be overcome, or to their use in particular problems. But no mention was made to the most serious fault of these methods, viz., that the muscle does not work under conditions which are physiologic. With the weight, the muscle is "loaded," having no interval of rest at any time, while with the spring it is "after-loaded." A large part of the energy expended by either the "loaded" or "after-loaded" muscle is not accounted for, because it is expended either in the form of internal energy or as external work which can not be computed. The loaded muscle, on the one hand, becomes tetanized early, and though the weight tends to stretch it during relaxation and the rest period, the results of such experiments with muscle-nerve preparations of a frog make it evident that the muscle neither relaxes nor rests between contractions after the fatigue sets in. The after-loaded muscle, on the other hand, must be exerting a certain amount of energy in "easing" back the weight to its rest which would otherwise fall back under the influence of gravitation. The cycle of the former is contraction, relaxation with load and stretching. With the latter it is contraction, relaxation with load and rest.

Put in a practical way, the loaded muscle might be explained thus: Let a man lift a twenty-five-kilogram weight from the floor to the table, and without resting it on the table lower it to the floor; but before it touches the floor let him raise it again to the table and repeat until he is exhausted. At no time does he rest from his weight, and fatigue comes on quickly. If, however, in the interval between the lowering and the next lift the weight is allowed to rest on the floor for a few seconds, the muscle will have a chance to recuperate, and he will be able to do more work as the result. This is the condition with the after-loaded muscle.

But neither of these forms of work is used by the muscles in active life. Therefore, any results or conclusions obtained by them under these conditions would be of limited value. What seems to me to be a better form of work might be explained thus: Let a man lift a weight from the floor to the table and leave it there, reach down and lift another and continue. Work is being performed by him only with the lifting of the weight. During the remainder of the time the muscles are relaxed and resting for the following task. Its cycle in work would be contraction, relaxation without load and rest. The muscles expend little or no energy during relaxation and none at all during the rest period. Fick, by means of his *Arbeit-sammler,* has applied this method to the frog muscle. Broca and Richet[13] have made a few experiments on the human muscle. Their work, however, has not been very extensive. Hall[14] applied this idea of Fick to the human muscle independently of Broca and Richet.

The above criticisms may be summarized as follows:

(1) The various forms of the Mosso ergograph "load" the muscle and cause it to exert energy in some form constantly, while work is being accomplished part of the time only.

(2) The spring ergograph "after-loads" the muscle when used to record isotonic contractions and allows rest for the muscle between relaxation and contraction, but not during relaxation.

METHODS.

With a view of overcoming as many of the objections as possible and applying this method of work to the human muscle, Hall's work-adder was devised. A detailed account of the instrument is necessary, as no description of it has ever been made in literature. By it the muscle works only during the actual lifting of the weight. The

---

[13] Broca and Richet: Experiences ergographiques pour mesurer la puissance maximum d'um muscle en régime regulier, Acad. of Sci. Comptes Rendus, 1898, p. 356.

[14] Hall: A New Form of Ergograph, Amer. Jour. of Physiol., vi, append. xxiii.

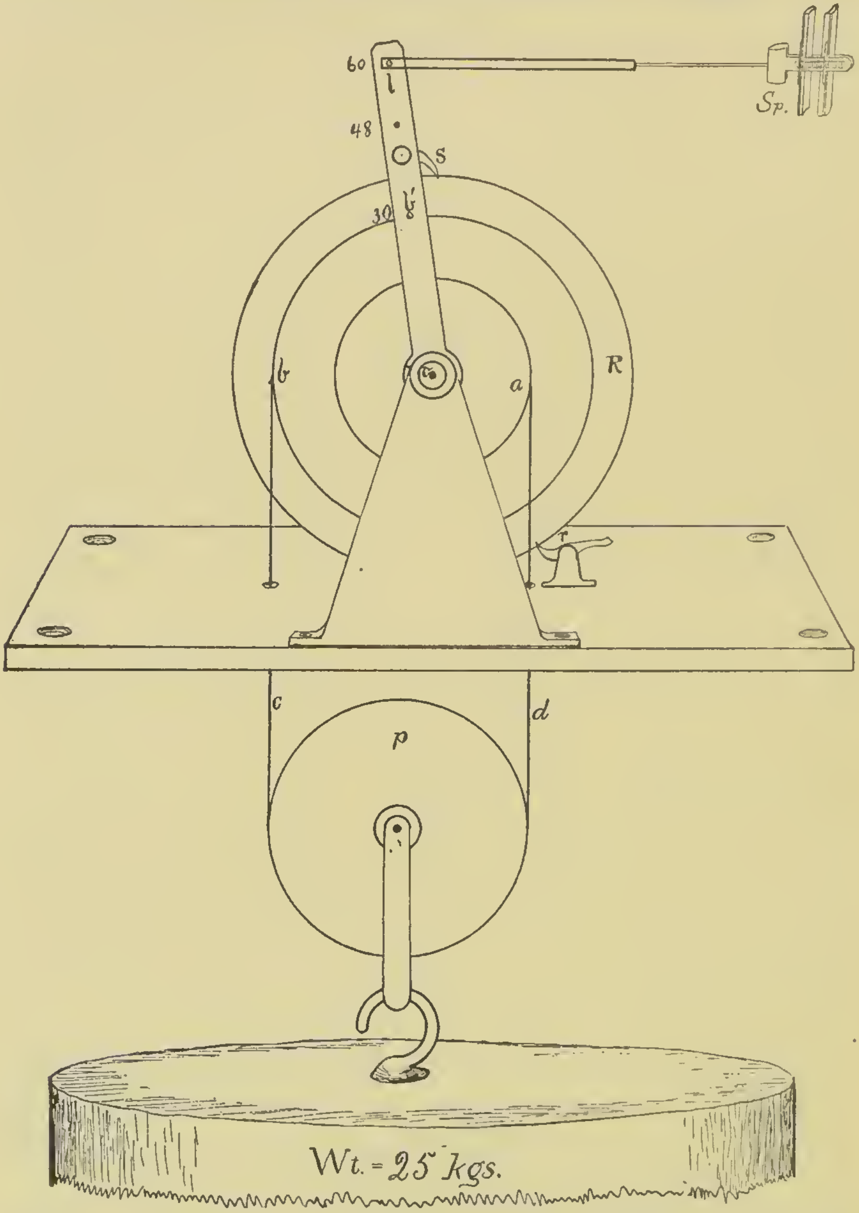


Fig. 1.—Diagram of work-adder. a, Small drum, 36 mm. in diameter; b, large drum, 60 mm. in diameter; cd, wire winding off drum a, around pulley p, and on to drum b; r, ratchet wheel, fixed immovably to both drums (this wheel has a toothed edge not shown in the figure); sp, finger splint or boot, which clamps the two terminal phalanges of the middle finger; r-s, ratchets (r fixed and s movable); l, the lifting or pulling lever, here set to lift at 60 mm. from the center o, thus lifting one-tenth of the weight, 25 kgs., as explained in the text. The splint may be attached to the lever at 48 mm. or at 30 mm.; in the latter case the amount lifted by the finger would be 5 kgs., or 11 pounds. Figure is one-half actual size.

troublesome inertia is lessened by having the weight made heavy and having it move so slowly that it follows the action of the finger very closely. Variations are allowed in the size of the weight by changing the leverage.

The objection may be raised that if the weight is of such large size, the finger, when nearly exhausted, will fail to move it, and there will be no record of the energy spent. But that the muscle may work to the full extent, a heavy weight is necessary. There are two kinds of work: (1) One in which the task is very great for that muscle and requires relatively an immense amount of energy to be expended with every effort put forth. This method can last for a short time only when exhaustion follows and a rest is necessary. (2) The other form is that in which the task is considerably below the working capacity of that muscle, and a relatively smaller amount of energy is put forth. The latter can be continued for a much longer time without fatigue necessarily following. Very different results follow the use of these two methods, and the distinction must be recognized when an interpretation of them is to be made. Some have failed to note this difference and considerable confusion has been the result. The formula—distance times weight—expresses accurately the amount of work a muscle can do if the conditions of the muscle itself and those under which it works are taken into account. Another objection is that the energy expended in starting the weights is greater than that to keep it going. This is true of every task and is not a valid objection if taken of every day work. Every object that a laborer lifts requires a greater expenditure of energy to start it than to keep it going. When the task is too great for him, he gets no credit for his work, but he still has energy sufficient for a task that is within his strength. The same principle should be applied to the individual muscle. Hough[15] admitted that "the work of our muscle consists for the greater part

---

[15] Cf. pp. 242 to 245.

. . . in a series of liftings of an approximately constant weight and that this weight is far below the maximum for a given muscle," and also says: "It would be a serious mistake to abandon altogether this type of instrument," viz.: weight ergograph in fatigue experiments.

It is true that the muscle under normal physiologic conditions is neither loaded nor after-loaded, as these terms are usually understood. It is not under a constant tension as when it contracts isotonically; it varies its length, differing from the muscle contracting isometrically. "During normal physiologic conditions a muscle does not contract isotonically, but always with a change of tension."[16] Expressed affirmatively, the working muscle expends energy only while it is lifting the weight; it varies its tension and rests between lifts. I have chosen to call a contraction under these conditions "normotonic."

THE WORK-ADDER.

One of the ergographs used in these experiments consists of a weight and a movable pulley suspended by a fine wire (Fig. 1). The two ends of this wire are wound in opposite directions on two drums (*a* and *b*) of different sizes. These drums are fixed on the same movable axis (*o*), and any movement will wind up the wire on one drum while it unwinds from the other. A ratchet (*r*) prevents any turning except in the direction which winds it on the larger drum, thus raising the weight. A pulling lever (*ol*) also rotates freely about the same axis (*o*), and by means of a ratchet (*s*) revolves the drum in the direction which raises the weight. The pulling lever then returns by the aid of a weak spring, with the finger, to its original position and is ready for the next pull. Complete rest is thus obtained for the muscle while it is not actively pulling. The heavy weight with the drums overcome, to a great extent at least, the inertia. The system of levers reduces the actual weight raised to within the power of the contracting muscle and allows for variation in its size.

---

[16] Schenck and Gruber: Human Physiology, p. 188.

The leverages are explained thus, as shown in Figure 1: The small drum (*oa*) has a radius of 18 mm. and the larger (*ob*) a radius of 30 mm. Each end of the wire (*c* and *d*), wound on these, supports one-half of the weight or 12.5 kgs. The drums act as levers of different lengths, and as each is supporting 12.5 kgs., the tendency is for the wire around the larger drum to unwind because of the longer weight arm. This movement is prevented by the ratchet (*r*). The exact amount of downward pressure to balance the 12.5 kgs. on (*oa*) is shown by the proportion, 30 :18 : :12.5 :x, or 7.5 kgs. But there is a weight of 12.5 kgs. hanging on the lever (*ob*). Therefore, the ratchet is sustaining the difference between 12.5 kgs. and 7.5 kgs, or 5 kgs., and before the weight can be raised this must be overcome. To further reduce this weight of 5 kgs. the pulling lever is used. The power arm (*ol*), which may be varied at will, is 60 mm. long, and the weight arm (*ob*) is 30 mm. long, the proportion being 60 :30 : :5 :x, or 2.5 kgs. Then the actual force necessary to raise 25 kgs. by this instrument is a force in excess of 2.5 kgs. pulling at the distal end of the pulling lever (*l*).

The arm rest consists of a slanting board modeled at the end to fit the hand. That the middle finger might have free movement, a notch was cut in the board. Straps hold the arm, hand and fingers in place. The first, third and fourth fingers are bent over the end of the rest and held in the partly flexed position by the straps. This allows the contracting muscle to pull the working finger toward the position held by the others instead of away from it and gives an easier movement.

This instrument fulfills the requirement (1) that the muscle works only when pulling the weight upward; (2) that the tension varies; (3) that the inertia be reduced and (4) that the muscle be neither loaded nor after-loaded. But the mechanical construction is at fault since the heavy weight after being raised to a distance of 50 cm. must be lowered again before the work can be continued again, thus allowing a rest for the muscle. Therefore, while it is suitable for ordinary fatigue work, it is not adapted to recording continuous efforts. That the experiments might continue with the same idea in view, another instrument of different mechanical construction, but involving the same principles, was made and substituted. Its construction and methods of work will be given.

THE AIR CUSHION.

The essentials of this instrument consist in an upright cylinder (see Fig. 2, *c*) closed at the lower end except for a large inlet valve (*a*) and at the upper end by a very thin sheet of dentist's rubber dam loosely stretched across it. A stopcock (*b*) is placed in one side of the cylinder. The weight while resting on the rubber sheet is not supported by it, but by a small metal bar (*d*) which strikes the frame. The action is as follows: As the weight is lifted from the cushion, air rushes in through the valve (*a*). When it is lowered, it strikes the rubber sheet and causes an increase of pressure within. This compressed air acts as a support until its slow escape through the stopcock (*b*) allows a return of the normal pressure within and the weight to be lowered, until it is caught by the metal bar. The rapidity with which it is lowered is regulated by the size of the opening made by turning the stopcock.

A wire extends from the weight up to an elbow lever (*l*) fixed at the end of the arm rest, and another extends horizontally from this to the finger where it is attached by an adjustable metal splint or boot (*sp*). The tracing lever records the actual movement of the finger on the drum (*D*). The size of the weight is easily changed by varying the length of the two arms of the elbow lever. The arm rest used was similar to the one described with the work-adder.

In previous ergographic work much attention has been paid to the character of the individual tracing and to the production of fatigue. In general, not over one hundred contractions were necessary to bring on this fatigue. But very little study has been made to ascertain under what conditions a muscle can continue to

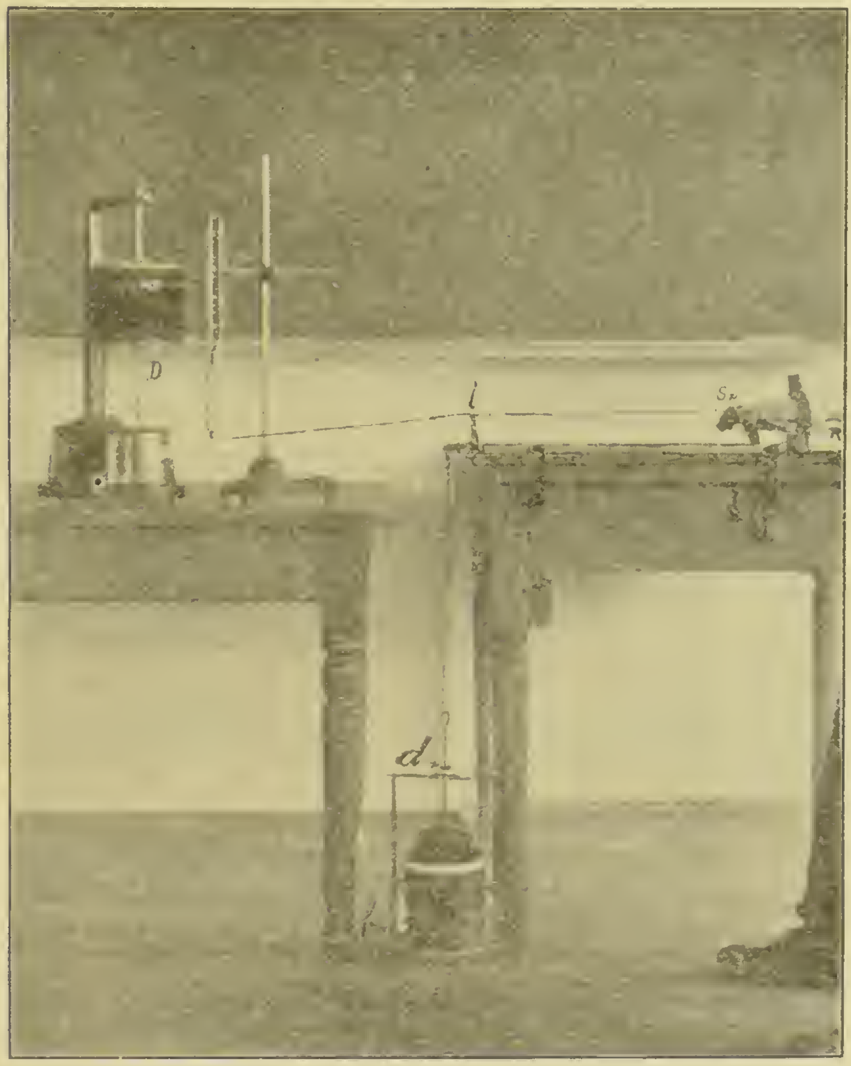


Fig. 2.—Ergograph with air-cushion. C, cylinder, about 10 cm. in diameter, having a large valve (a) opening from below; b, stopcock through which the air escapes on descent of the weight, the rate at which it escapes is regulated by the stopcock; d, metal bar soldered to the weight rod, this bar strikes the cylinder frame and serves to support the weight between contractions; l, elbow lever, so constructed that the two arms may be varied in length by hooking the weight cord or the power cord into different holes: Sp, finger splint; R, arm rest; D, drum of kymograph.

work for a long period of time. In 1890, Maggiora[2] found that he could contract the middle finger of his left hand continuously at the rate of one contraction in two seconds against a weight of 1 kg. He concluded from his experiments that there exists for the human muscle a definite weight with which one can perform the greatest possible work. When the weight or the rate of contraction is increased, fatigue will occur. He also found that this maximum of work varies with different persons at the same time and the same muscle at different times. Lombard[3] contracted the abductor indicis muscle about 9,000 times, or for two and one-half hours, at the rate of once a second against a weight of 500 gms., reaching about the same conclusions as Maggiora. Both of these investigators used the weight ergograph which loaded the muscle and did not allow the muscle to work to the greatest advantage. Maggiora flexed the entire finger while the hand was in the supine position. Neither seems to have tried to compute the amount of work done by these muscles.

Fick[17] found that, using a heavy weight, about one-fourth of the total energy expended by a muscle is used in lifting it and the remainder is changed into heat, electricity, etc.; while with a light weight, only about one-twentieth is spent as external work. That there is so much loss of energy is due, I think, to the fact that the muscle does not work to the greatest advantage. While some attempts have been made to improve the condition under which the muscle works, sufficient data have not been tabulated to show the true value of these changes.

The results given here were obtained principally on the air cushion. That the muscle might be in training, as Hough[18] has shown is necessary for the best results, the experiments were continued over a period of two months in the spring of 1902 and about three months in the spring of 1903. Tracings were made at least every other day. While the experiment was being made, the subject sat at a table with the right arm and hand fastened in a prone position to the rest. Different weights were used, the rule being to increase them as the finger becomes accustomed to the work. At first the muscle became tired very quickly, but after a few weeks it gained in power and could use the heavier weights at a faster rate of contraction. The rhythm was usually a matter of choice and was influenced largely by the object in view. While many found that they could bring on fatigue within one-hundred contractions at the rate of one contraction every two seconds, I found that I could go at a much faster rate and continue a very much longer time without fatigue necessarily following. The height of the contractions remained practically the same, varying from 1 cm. to 1.5 cm. in height. Throughout the experiments care was taken to keep the nutrition of the finger and muscle as nearly normal as possible. No attempt was made to compute the friction, which was comparatively small. Tension on the muscle was present only during the lifting of the weight.

---

[17] Fick: Pfluger's Archives, 1878, xvi, p. 85.

[18] Hough: Ergographic Studies in Muscular Soreness, Amer. Jour. of Physiol., 1902, vii, p. 76.

Table 1 shows some of the results obtained.

Part A of Table 1 shows the results of the experiments on the work-adder. The longest single experiment was made May 8, and lasted for a period of three hours and forty-seven minutes, during which time over 11,000 contractions were made, and about 625 kilogram-meters of work accomplished. May 10 two tests were made with an interval of one hour and thirty minutes. The work done that day amounted to over 1,000 kilogram-meters. No fatigue other than a general body weariness was experienced after these experiments, and the height of the contraction remained very constant throughout each experiment. But the experiments were not above criticism, as there was some movement of the whole finger, and intervals of rest were made necessary when the weight was lowered.

Part B of Table 1 shows the work accomplished on the air cushion. March 28 I made 12,600 contractions in three and one-half hours. The rate was one contraction every second against a weight of two and one-half kgs. The average height of each of the tracings was 1.1 cm. and the total work accomplished 346.5 kilogram-meters. No fatigue occurred. On April 1, the rate of contractions was changed to 2 per second and the weight to 3 1/3 kgs. It was thought that this would bring fatigue; but to my surprise, after some irregularity in the tracing, the height of the contractions became more even and no fatigue was produced in two and one-half hours. The next tracing was made at the rate of two contractions a second with a 5-kg. weight. The tracing was regular for nine minutes, then varied considerably in height until fatigue (a failure to move the weight) came on at the end of forty-two minutes.

TABLE 1.

Date.	Time of Day.	Duration of Experiment, hrs.-min.	Weight in Kilograms.	Contractions per Second.	Average Height of Contract's in cm.	Number of Contractions.	Kilogram-meters of Work Done.
A.—RESULTS OBTAINED ON THE WORK-ADDER IN SPRING OF 1902.							
May 8, 1902....	8 :12 a. m.	3 :47	2.5	1	2.2	11.370	*625.35
May 10, 1902...	8 :45 a. m.	3 :23	2.5	1	2.15	10,180	*547,175
May 10, 1902...	1 :30 p. m.	2 :58	2.5	1	2.2	8,930	*479,987
B.—RESULTS OBTAINED ON AIR-CUSHION IN SPRING OF 1903.							
March 28, 1903..	2 :15 p. m.	3 :30	2.5	1	1.1	12,600	*346.5
March 31, 1903..	10 :20 a. m.	1 :00	2.5	2	1.1	7,200	*198.
April 1, 1903....	8 :15 a. m.	2 :30	3 1/3	2	1.1	18.000	†660. (?)
April 2, 1903....	3 :30 p. m.	0 :42	5	2	(?)	5,040	‡ ......
April 4. 1903....	8 :20 a. m.	3 :40	3 1/3	2	1.1	26,400	*968.

* No fatigue. † Some irregularity. ‡ Tracing irregular after 9 minutes; fatigue in 42 minutes.

On April 4 the weight was changed back to 3 1/3 kgs., and with the same rate 26,400 contractions were made in three hours and forty minutes. The contractions varied between 1 and 1.4 cm., with an average of about 1.1 cm. Not over twenty-five strokes were lost during the entire time, and the wide variations to be expected from weariness or disturbances were surprisingly absent. No fatigue occurred except a general weariness of the whole body, which lasted during the remainder of the day. The weariness did not stop the work of the experiment, however. The total amount of work was over 968 kilogram-meters. The tracing is shown in Figure 3.

Comparing this last tracing with that of April 2, it will be seen that the heaviest weight that this muscle can lift continuously, contracting twice a second, is between 3 1/3 and 5 kgs. No similar amount of work has, to my knowledge, been recorded previously by a single muscle. This apparent increase of ability must be due, in a great measure, to the more advantageous conditions under which the muscle is working. Just how long this work could have continued I will not venture to say definitely, but the fact that I could keep up this pace for three hours and forty minutes without fatigue of the muscle following would justify the conclusion that the muscle could have done more. It is evident in the above experiment that the muscle had sufficient rest after each contraction to recover from the effects of that contraction. Had this not been the case fatigue would have been the result, as it had been with the use of the 5-kg. weight.

Since so many factors enter in to modify the conditions, it is not to be expected that the results will be the same in each experiment; but with the conditions sufficiently favorable it may be concluded that a muscle is able to do a day's work of eight or ten hours' duration.

FATIGUE.

Mosso,[1] Lombard,[3] Maggiora[2] and others found that the muscle became tired and could not lift a given weight after from 50 to 100 contractions, the rate being once a second. With them, the amount of work, as well as the extent of movement, decreased as fatigue was approached. Franz[19] found that with the spring he could contract 150 times and still do about 40 per cent. as much work as at the beginning of the series. During the present experiments the muscle was fatigued several times and it always gave results far in excess of those obtained by these men. The muscle did not become fatigued within a period of three hours and forty minutes when it raised a 3 1/3-kg. weight twice a second. On April 2 the muscle became fatigued in forty-two minutes after having made over 5,000 contractions against a 5-kg. weight, lifting it twice a second. After a lapse of about four weeks, it made nearly 4,000 contractions under the same conditions.

That I might find a cause for this great difference in ability, I made a few experiments with the Mosso form of ergograph. Table 2 shows some of the results as compared with those taken with the air cushion.

TABLE 2.

Date. 1903.	Contraction Length of in Minutes.	Weight Used.	Contractions per Second.	Number of Contractions to Fatigue.	Results.
RESULTS WITH AIR-CUSHION.					
April 2	42	5	2	5,040	fatigue
April 4	220	3 1/3	2	26,400	no fatigue
April 29	33	5	2	3,960	fatigue
RESULTS WITHOUT AIR-CUSHION.					
April 5	22	3 1/3	2	2,640	fatigue
April 16	24	3 1/3	2	2,880	fatigue
April 29	1 :08	5	2	135	fatigue

These tracings compare the time and work necessary to produce fatigue when the air cushion is used and without it.

These results do not agree with those obtained by the previous investigators. With a weight of 3 1/3 kgs. twice a second, there was no fatigue until 2,640, and in

---

[19] C. f., p. 368

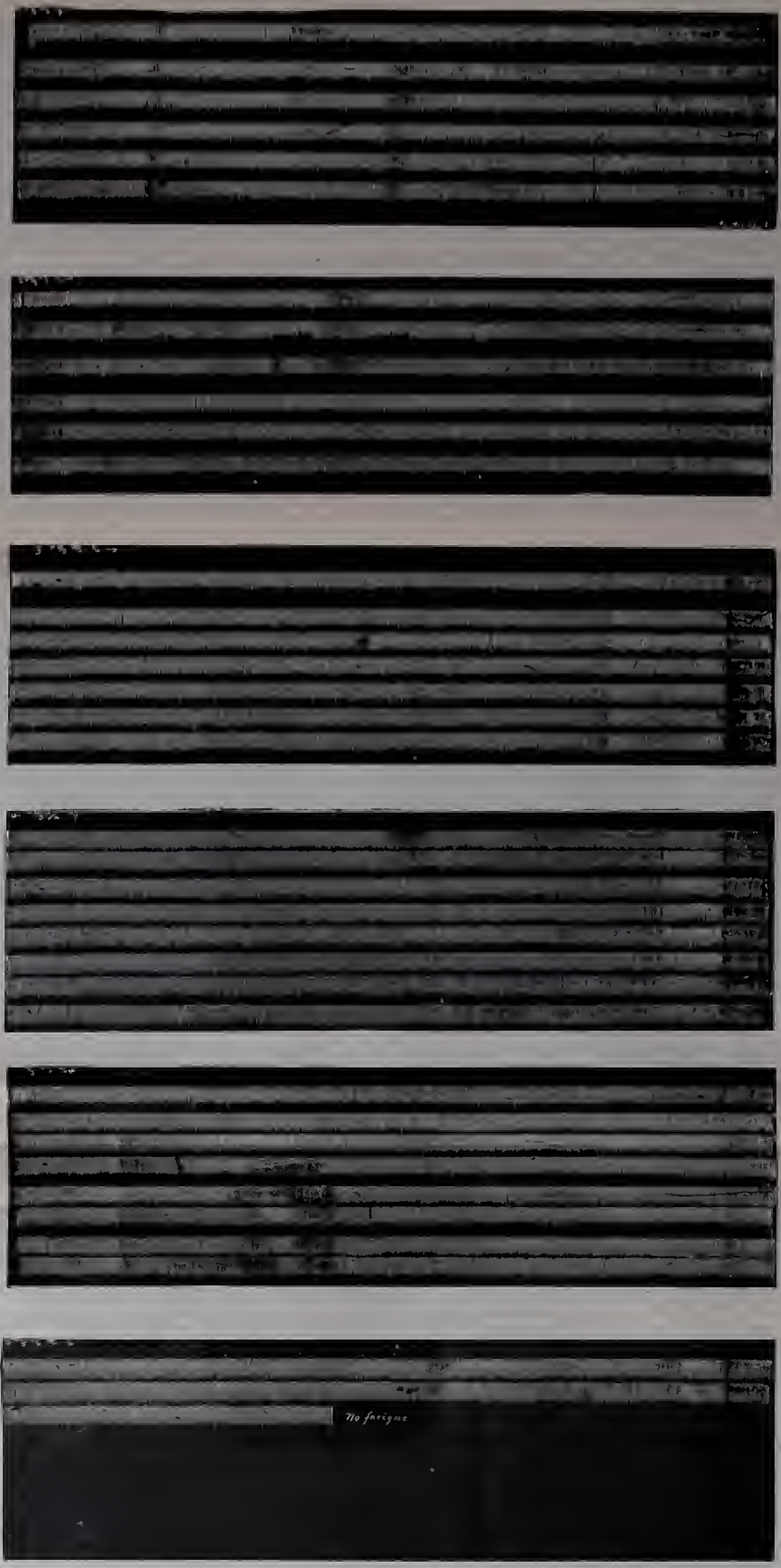


Fig. 3.—The record of an experiment performed on April 4. 1903. in which a weight of 3 1/3 ko. (7.3 lbs.) was lifted by last 2 phalanges 3d digit of the right hand 26.400 times in 3 hours and 40 minutes. the total work done exceeding 971 kilogram meters. At the end of the half day's work the finger was not fatigued.

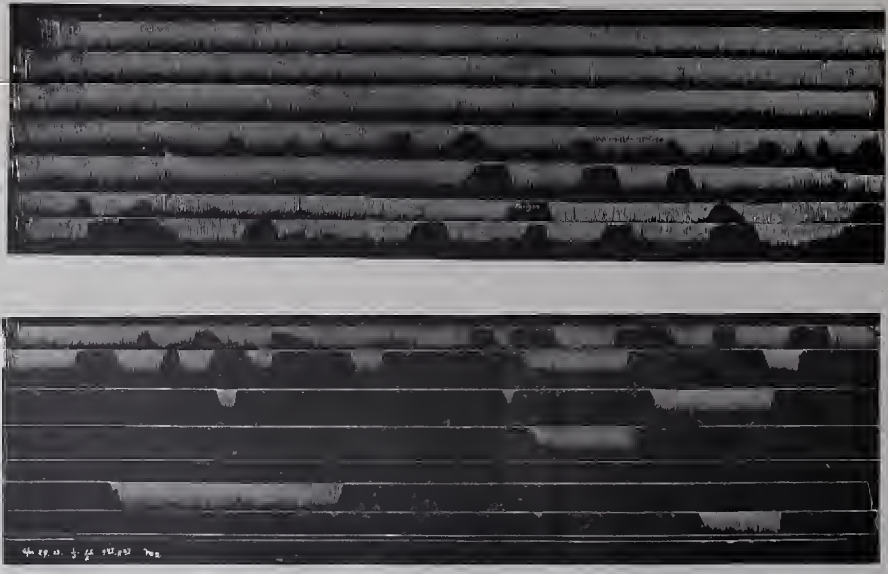


Fig. 4.—Tracing taken during an experiment in fatigue. The tracing shows alternating recovery and fatigue. During the whole period of the experiment (1 hour and 10 minutes) there was an attempt to contract the finger to the maximum. Note that in the fourth round of the first drum the beginning fatigue makes itself manifest in the groups of short contractions. The first complete fatigue is not reached past the middle of the sixth round, marked "fatigue" on the tracing. During a large part of the time consumed in the last eight rounds of the second drum the flexor muscles of the finger were unable to make the slightest contraction, though the attempt was made each half second by the subject.

another 2,880, contractions had been made. At another time the muscle, contracting every half second, raised a weight of 5 kgs. 135 times before fatigue was produced.

The question arises, why there should be such a difference in the amount of work necessary to produce fatigue? The individual variations of the muscles would easily explain small differences, but would not suffice here. The muscle that I used was below the average in strength before the experiments began, and the time over which the experiments extended would scarcely allow such great increase in power. The difference which exists between the tracings made with the air cushion and those with the Mosso form of ergograph can be explained to a great extent by the conditions under which the muscle was working. The other is evidently the result of the endurance which the muscle gained by working many times over an extended period.

RECOVERY AFTER FATIGUE.

It was also noticed that the periods of recovery after fatigue had been reached were very much longer when the air cushion was used, than when the Mosso form of ergograph was used. The average number of contractions in the recoveries of an experiment lasting one hour and forty minutes was eighty-five, and the average intervals of absolute fatigue was fifty seconds, varying in length from 2 to 10 cm. The weight used was 5 kgs., raised every one-half second. There was no regularity in the length of the recoveries, while the intervals of loss of power had a tendency to become longer as the experiment was continued. A tracing of this experiment is shown in Figure 4. For a detailed discussion of this subject the reader is referred to the work of Lombard.[20]

---

[20] Lombard: The Effect of Fatigue on Voluntary Muscular Contractions, Jour. of Psychol., 1890, vol. iii.

SUMMARY.

1. A muscle working under normal physiologic conditions is neither "loaded" nor "after-loaded."

2. A muscle will not contract isotonically nor isometrically under normal physiologic conditions.

3. When a Mosso or a spring ergograph is used, a large part of the energy expended by a muscle during a period of work is lost. This loss occurs in easing back the weight or the spring to its position of rest or to the zero point.

4. A recognition of the conditions under which a muscle works and the end to be attained is necessary when an interpretation of ergographic results is to be made.

5. A normal muscular contraction ("normotonic") consists in contraction, relaxation without load, rest.

6. A new form of weight ergograph has been devised which allows the human muscle to work at a greater advantage than that given by any previous form of ergograph, because it permits "normotonic" contractions.

7. A human muscle is capable of doing a far greater amount of work by the use of the new ergograph than has been previously shown in ergographic work.

8. A muscle can work over periods of long duration without fatigue when the conditions are favorable.

9. These experiments confirm the conclusion stated by Maggiora that there is a definite weight with which one can perform the greatest possible work.

10. The physiologic limit of a muscle for continuous work is modified by the rate, load and interval, or by rest and work.

NEW PHYSIOLOGIC APPARATUS.

THE FROG-BOARD MYOGRAPH AND THE MANOMETER TAMBOUR.

WINFIELD S. HALL, M.D.
Professor of Physiology, Northwestern University Medical School.
CHICAGO.

THE FROG-BOARD MYOGRAPH.

The term myograph was originally applied to the whole apparatus used in recording the contraction of a muscle. The pendulum myograph of Helmholtz included the muscle-clamp, the muscle-lever and the moving surface (pendulum) on which the myogram or muscle-tracing was recorded. After the rotating cylinder came into use as a recording surface under the name of the kymograph, the term myograph has been applied to that portion of the apparatus which represented the muscle-clamp and the lever with the load and the tracing point. Such an apparatus traces on the kymograph the muscle-curve or myogram.

The myograph has taken several forms: In the simple myograph of Helmholtz, in the muscle-signal of Du Bois Reymond, and in several other forms the muscle is exposed to the atmosphere. The changes wrought by the atmosphere soon put the muscle-nerve preparation into an abnormal condition and the responses to stimuli are not typical. In fact, the evaporation of moisture soon condenses the tissue-plasma sufficient to induce a typical "salt-tetanus." The application of normal saline solution can temporarily, but only temporarily, avert such a result.

To reduce to a minimum the effect of atmospheric changes the so-called "moist-chamber" was devised. This consists of a glass chamber which enclosed the muscle and nerve and the electrodes with the muscle clamp. A wire or thread passes through the bottom of the chamber to the tracing lever. The air in the chamber is kept saturated with moisture by a wet paper or sponge within. This device overcomes to a large extent the difficulties with which one must contend in attempting to work with the exposed muscle. There is one serious difficulty, however, which has not been mentioned and which is not corrected by the moist-chamber myograph, namely, the cutting off of the muscle from the blood and lymph circulation. In the classic method of making a muscle-nerve preparation from the gastrocnemius muscle and sciatic nerve of the frog, the muscle and nerve, with a portion of the femur, are completely removed from the frog's body, thus not only exposing them to atmospheric changes, but removing them completely from connection with the circulatory system.

For fundamental experiments on the elementary tissues, and for work with drugs in pharmacology, it is of very great importance to have a myograph that is simple and inexpensive and which does not involve disturbing the circulatory system. The importance of the last point can not be over-estimated. The circulatory system not only brings a continuous supply of nutriment and oxygen to the muscle, but carries from the muscle the accumulating products of fatigue and thus enables the muscle to do much more work than would otherwise be possible.

In pharmacologic experiments it enables the experimenter to watch the influence of drugs carried to the muscle in the normal way, rather than applied in some artificial and abnormal way.

The frog-board myograph is a new form of myograph so constructed as to permit all experiments usually performed on the gastrocnemius-sciatic preparation without exposing the active tissues to the atmosphere or disturbing the blood supply. The instrument is constructed as follows: An oaken base about one-fourth of an inch in thickness supports a cork plate of equal thickness; the cork plate presents a surface about 10 by 25 centimeters. (Fig. 1.) The lever holder at the end of the plate is constructed of thin sheet steel and slips from side to side in order to bring it opposite either leg of the frog.

The distance from the axis of the elbow-lever to the thread-eye is the same as that to the weight, therefore, the weight lifted by the muscle is the actual weight hung upon the weight link. When the lever passes a little below the horizontal position it comes into contact with the rest. This rest can be used in "after-loading" a muscle. For further description of the instrument, see the figure and its description.

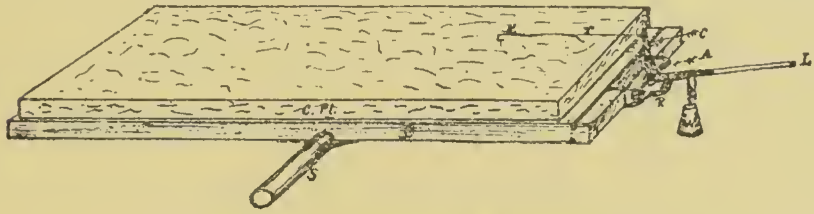


FIG. 1.—FROG-BOARD MYOGRAPH.

S, the shaft which is clamped to the upright stand; B, the oaken base; C. Pl, the cork plate to which the frog is fixed; A, the lever axis and slide lever-holder; W, the weight; L, the light lever about 20 cm. in length; H, the tendon hook which is joined through the thread T, which passed through the eye and under spring catch (c); R, the lever rest.

In the use of the frog-board myograph one proceeds as follows: The frog is pithed and pinned, dorsum up, on the cork-plate, with the feet at the lever end. The tendo-achillis is exposed and loosened from the tarsal ligaments, the tendon-hook (H) is passed through the tendon and the length of the thread adjusted at (c). The skin on the thigh is opened to the extent of two centimeters and the biceps femoris muscle removed, the sciatic nerve carefully separated from the sciatic artery and placed on the insulated electrodes. Stimulation may be made from time to time for a period of several hours before the preparation becomes exhausted.

SUMMARY.

1. The frog-board myograph is a convenient and inexpensive myograph especially adapted for work in general physiology and in pharmacology.

2. Its advantages over other similar instruments are as follows:

I. The muscle-nerve preparation can be made in at most one-fourth the time required for the classic preparation.

II. The muscle and nerve are not exposed to atmospheric changes.

III. The circulation of the tissues is not disturbed. This has the advantage (1) of permitting the study of the action of drugs on muscle-tissue under normal conditions, (2) of studying fatigue without the accumulation of fatigue products under abnormal conditions.

THE MANOMETER TAMBOUR.

The second piece of apparatus to which I propose to call your attention is the manometer tambour (Fig. 2).

A very large number of research problems require the recording of blood pressure of the animal—rabbit or dog—under observation. In the physiologic or in pharmacologic laboratories where such observations are in progress almost daily, it is not difficult to get very satisfactory results with the classic apparatus, which consists of a mercury manometer whose proximal tube (p) is joined through the medium of pressure tubing (p t) to the canula (e), the pressure tubing being interposed at (T) by a T-tube, one limb of which passes to the reservoir containing a one-half saturated solution of $MgSO_4$ or some other agent for retarding coagulation. Into the distal limb of the manometer (d) there is fitted, in the classic apparatus, a float which rests on the mercury, following more or less accurately the variations in the level and carrying a vertical rod which slides through a guide in the upper end of the distal limb and bears at its upper extremity a horizontal reed, bearing at one end a tracing point.

There are two serious difficulties with this float. First, it is likely to fail to work properly just at the time when you are most anxious that there should be no hitch in your observation, though if the apparatus is in almost daily use this difficulty is not a serious one. The serious objection against the float is, that it does not follow accurately the movement of the mercury. The mercury starts up a little before the float does, and the

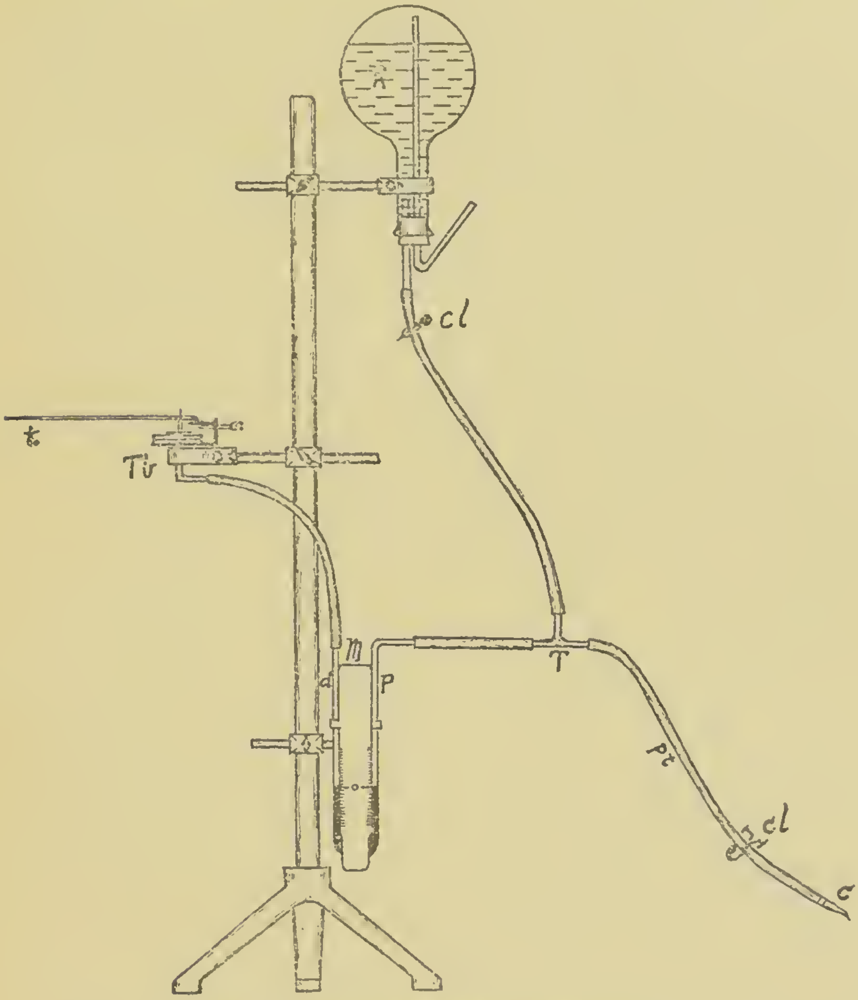


FIG 2.—THE MANOMETER-TAMBOUR.

M, manometer; Tb, tambour; R, reservoir filled with ½ sat. sol. $MgSO_4$; T, T-tube; Pt, pressure tube; Cl, clamp; C, canula; P, proximal limb of manometer; D, distal limb of manometer; T, tracing point of tambour lever.

float itself has so much inertia that the actual movements of the mercury are not shown at all by it. In order to overcome this difficulty, and to be able to record accurately the movements of the mercury meniscus, the following variation of the classic apparatus was contrived.

A small tambour was joined to the distal end of the manometer by a piece of pressure tubing and supplied with a very delicate tracing lever which magnifies the movements of the membrane 10 or 20 times, as desired, the levers being variable in the construction of the instrument. The surface of the tambour should not be larger than 15 mm. in diameter. The diameter of the mercury meniscus should probably be not less than 3 mm. in diameter. With this ration between the two surfaces and the levers multiplying 10 to 20 times, the most beautiful arterial pressure tracing can be obtained, showing not only the respiratory and percussion waves, but also the dicrotic wave clearly superimposed on each cardiac wave.

This apparatus, as above described, has one limitation which may, for certain kinds of work, seem to be a disadvantage. The pressure tubing leading from the distal end of the manometer to the tambour (Tb) is not attached to the manometer until after the rise of the mercury in the distal tube following the removal of the clamp (cl). After the tambour is attached to the manometer every movement of the mercury is shown by corresponding movements of the tracing point (t). Should there be a sudden rise or sudden fall of pressure, it will be instantly and clearly shown by corresponding rise or fall of the tracing. Should there, however, be a very gradual rise or a very gradual fall, owing to physiologic changes in the tonus of the blood vessels, for example, or perhaps by the gradual action of some drug on the animal under observation, this will not be shown by corresponding rise and fall of the tracing. It will, however, be shown by the stand of mercury in the distal limb of the manometer, and this may be easily read off or noted from time to time.

To offset this slight disadvantage, one has the two advantages above mentioned, namely, accuracy of the tracing of all the quicker movements of the mercury and the assurance that one's apparatus will always work.

REPORT ON THE SCIENTIFIC EXHIBIT

OF THE AMERICAN MEDICAL ASSOCIATION, AT NEW ORLEANS, MAY 5-8, 1903.

FRANK B. WYNN, A.M., M.D., Chairman.
INDIANAPOLIS.

The fourth Scientific Exhibit of the Association was most successfully consummated, despite obstacles which for a time threatened a favorable outcome. The remoteness of New Orleans from sources of material and a three-month period in which to accomplish the work, cast a gloom over those deeply interested in the continued success of the movement. Too much can not be said in praise of those who came nobly to the rescue at a critical time. On the roll of honor are twenty-eight persons who labored faithfully, without money and without price, for the common good of the profession and the success of the meeting. Among them are those distinguished both in the scientific and practical fields of medicine, as well as young men fired with enthusiasm for the higher ideals of the profession.

In a perusal of the subjoined report it will be noted that 16 well-known colleges, hospitals or public institutions are represented and 11 private collections. The analytical reader will observe as conspicuous features three research exhibits and the general tendency of contributors to the grouping of specimens in illumination of particular phases of pathology. This is in response to the gradually evolved policy of the committee.

Lack of efficient demonstration has long been recognized by those having the matter at heart as the weak point of the exhibit. Many specimens extremely valuable as practical object lessons, remain impotent on the shelves unless intelligently demonstrated. As long as five years ago the writer, in a letter to The Journal, strongly advocated systematic demonstration in connection with the presentation of state society exhibits. It is just as important for national collections if the greatest degree of instructive efficiency is to be attained. It was hoped in the outset that exhibitors would see to the demonstration of their own contributions. Few, however, have been able to give so much time. The plan has also been tried of attempting to secure a large demonstration corps of medical students and young physicians resident in the place of meeting, who should alternate in escorting small delegations of visitors about the exhibit. But it was found impossible to secure a sufficient number of competent men willing to give the necessary time. The solution of this perplexing problem has come naturally in the reduction of the size of the exhibit and its specialization. In this way demonstration becomes simplified and less laborious.

The particular phases of pathology or other scientific branch of medicine illuminated in the exhibit from year to year should be varied according to the topics prominently before the profession and likely to command conspicuous attention in the Section meetings. In consonance with the ideas expressed there were shown at New Orleans very complete series illustrative of the following: Anomalies and pathologic conditions of the heart; tuberculosis in the various organs and structures of the body; amebic dysentery with sequels and intestinal lesions of tuberculosis and typhoid for purposes of differentiation; malaria; fibroid tumors; ectopic gestation; surgical diseases of the kidney; pathologic conditions of the bladder and prostate gland; renal and vesical calculi; otologic and neurologic groups. Effort was made to have these series demonstrated before the interested sections in conjunction with related papers to be read. The idea met with warm reception on the part of Section officers generally, but crowded programs made its consummation difficult of accomplishment. For the coming meeting at Atlantic City, however, it may be definitely stated that demonstrations of particular series of the exhibit will be conducted by persons of distinction, scheduled for specific hours and days on the published program.

M'GILL UNIVERSITY: GEORGE ADAMI AND M. E. ABBOTT.

1. *Ruptured Tubal Gestation, Third Week.*—Age 26; two full-term children, last one being 4 years of age. Menstrual history: Began at 12; regular; scanty, only lasting one and one-half days. Complaints on admission: Sudden, severe pain in the lower abdomen and fainting on Dec. 1, 1902, lasting until operation on the third. Last regular period Nov. 15, 1902, but since then any exertion would cause flow. Nauseated two weeks and had two chills the day before operation. Pulse weak, thready, 168; respirations, 44, labored; temperature, 98 2/5. Operation Dec. 3, 1902. Abdominal cavity contained a large quantity of fluid blood. Recovery.

2. *Tubal Pregnancy. Rupture in Early Weeks.*—Aged 26. Last labor eight months previous. Last regular period June 13, 1900; menstrual flow from May 17 to June 3, with severe pains in abdomen, persisting until June 13, when they became very severe and collapse developed. Pulse, 115; respirations, 44. Abdominal section. Recovery.

3. *Ectopic Gestation.*—Specimen a five and a half months fetus, which had remained in the abdominal cavity seventeen years, having been killed by application of electricity. Fetus now represented by a mass bent on itself, the bones of vertebral column, ribs, one upper extremity and part of cranium still plainly made

out. Patient aged 55. In 1885 right tube found to be seat of gestation of five and one half months. Gestation was checked by application of electricity. For eight years the patient was well, but for the past nine she has had recurring spasmodic pains, growing worse and worse. Abdominal section Dec. 13, 1902. Recovery.

4. Fetus, Sac and Tube. Ectopic Gestation, Five and One-half Months.—Patient aged 30. Complained on admission of epigastric pain, vomiting and weakness. Pulse, 160; respirations, 36; temperature, 98.8 F. Last menstruation Jan. 26, 1901. Usual signs and symptoms of pregnancy marked. During night of July 3 was seized with paroxysms of epigastric pain and vomiting, followed in some hours by a chill. On July 4 had three fainting spells. Pelvic examination revealed a soft cervix, to which was attached a firm globular mass. Neither ballotment nor rhythmic contractions could be felt. Operation July 4, 1901, revealed fetus floating in free blood in the abdominal cavity. Recovery.

5. Tubal Pregnancy. Ruptured in Third Month.—Enlarged uterus and appendages; the right tube enlarged to form tumor size of an orange; laid open to show placental tissue, fetus and cord *in situ.* Fetus apparently dead some time. Pelvic hematocele and septic peritonitis. Patient aged 32; amenorrhea and morning vomiting for three months; severe crampy abdominal pains, with bloody vaginal discharge for three weeks before death from septic peritonitis.

6-9. Ruptured Tubal Pregnancies.

10. Section Through Pelvic Organs, Showing Multiple Fibromata Uteri, with Calcification.

This beautiful exhibit was solicited as a special feature in illumination of ectopic gestation, which was one of the topics prominently considered by the Section on Obstetrics and Diseases of Women. It was the second contribution of McGill University to the Scientific Exhibit of the Association, and testifies most forcefully to the scientific spirit and friendly cooperation of our Canadian colleagues.

CINCINNATI HOSPITAL AND CINCINNATI ACADEMY OF MEDICINE: HORACE J. WHITACRE, ASSISTED BY J. C. BUTTEMILLER AND MARION WHITACRE.

In conformity with the suggestion of the committee the following contribution was arranged to illustrate chiefly one phase of surgical pathology, viz., surgical diseases of the kidney.

Nos. 11-78. Group I. Surgical Diseases of Kidney.—68 wet specimens, showing the following range of lesions: Contracted kidney; large white kidney; rupture of kidney (nephrectomy); cystic kidney (four varieties); pyelitis; hydronephrosis, from stone in ureter, from hypertrophy of prostate, from cancer of the vesical ends of both ureters, and from stricture of urethra; pyonephrosis (eight specimens); stone in pelvis of kidney (several varieties of stone); tubercular kidney; sarcoma of kidney; retroperitoneal sarcoma and carcinoma.

Especially beautiful in this group were two congenital cystic kidneys; also the series of tubercular kidneys. One specimen showed a definitely circumscribed tuberculous mass in one end of the organ; another great numbers of miliary tubercles; another multiple caseous foci varying in size from a pin-head to a large pea; a fourth was reduced to shell one centimeter thick; in a fifth the capsule formed a sac filled with caseous matter, but no demonstrable tubercular tissue; and a sixth constituted a tumor the size of a child's head.

Nos. 79-104. Group II. Calculi.—Removed from the pelvis of the kidney, from the middle of the ureter, from the vesical end of the ureter and from the bladder. Fifteen of these loaned by Joseph Ransohoff; others by J. C. Oliver, N. P. Dandridge and William Judkins.

The specimen of pyonephrosis with stone in the pelvis of the kidney presents some features of unusual interest. First a stone weighing six and one-half ounces was removed by operation; four weeks later the kidney was removed, as the patient did not improve. Later it was found that the kidney of the opposite side was totally destroyed and contained a large stone.

Nos. 105-110. Specimens of Ectopic Gestation.—Presented by Charles L. Bonifield and John Miller.

No. 111. Embolism of Left Coronary Artery.—This case occurred in the practice of Paul Millikin of Hamilton, Ohio. The patient, a young man, died with marked symptoms of angina pectoris. The necropsy revealed a ruptured chorda tendineæ protruding from the mouth of the vessel, while on the end within the artery was a small thrombotic mass completely occluding the vessel.

Not only from a pathologic standpoint was this collection most excellent and instructive, but in an artistic way as well. Most were Kaiserling preparations, mounted with great care. It was the third contribution from Cincinnati to the National Exhibit and constitutes a forceful example of the stimulating effect of the exhibit in awakening local interest in practical pathology. Three years ago the showing of Cincinnati at St. Paul was meager; at Saratoga decided improvement was noted; and the superb collection presented at New Orleans reflected great credit on the profession of Cincinnati, and gives proof of substantial progress in the field of practical pathology.

MEDICAL DEPARTMENT TULANE UNIVERSITY: O. L. POTHIER.

Nos. 112-219. Photographs.

This excellent array of photographs was designed to show more particularly the diseases prevalent in the colored race, such as keloid, leucoderma, elephantiasis, etc. One beautiful picture was of a most extensive case of pemphigus in the negro, followed by cure. Another photograph was of a case of pseudohermaphrodism, presenting a most interesting history. The individual was 45 years of age when admitted to the female wards of the Charity Hospital of New Orleans. He had always supposed himself a woman, and had always lived among women. It was by accident that the physician in charge discovered that the condition was simply hypospadias. The man refused to put on male clothing, and when transferred to the male wards took the first opportunity offered to run away.

No. 220. Double-Headed Monster.—A noteworthy specimen from a colored woman. She had traveled some distance from the country with one of the heads born. When admitted to the Charity Hospital the case was supposed to be one of twins which had become locked. As the first child (?) was dead, amputation of the head and shoulder was performed. Recognition of the monster came only with the birth of the other part. An examination of the monster revealed four lungs, two hearts, two stomachs, two duodenums for a distance of about an inch, after which they fused, and single intestine. There were two kidneys, one liver, one spleen, and the organs of reproduction single. The body showed two heads, two spinal columns, two spinal cords, fusion taking place at the sacrum, two arms and two legs.

No. 221. Elephantiasis of Penis.—The subject was a negro who presented no other evidence of the disease. The organ measured twelve inches in length and fourteen in circumference.

Nos. 222-235. Miscellaneous Gross Specimens.

The collection gave ample evidence of the richness of the field for the study of pathologic conditions more or less characteristic of the negro. New Orleans offers in the Charity Hospital a wealth of material which under the present efficient pathologic dissection will yield valuable results in the near future.

MEDICAL DEPARTMENT, UNIVERSITY OF TEXAS: W. S. CARTER.

Nos. 236-255. Apparatus.—Some twenty pieces for physiologic experimentation, largely constructed in the Harvard laboratories under Professor Porter, and partly devised in the laboratories of the University of Texas.

Nos. 256-315. Tracings.—Six books, very neatly made by students of the university and grouped as follows:

(*a*) Frog's heart and circulation: showing influence of cold and warm physiologic salt solution on heart beat.

Peculiarities of heart muscle: staircase contractions after first ligature of Stannius; latent and refractory periods; maximum contraction with minimum stimulus; separate contractions from tetanizing current, etc.

Innervation of heart: augmentation of heart beats from stimulation of sympathetic; stimulation of vagi and crescent normally and after application of nicotin; crossed action of muscarin and atropin on ganglia of heart, etc.

Blood pressure in aorta: effect of cardiac inhibition of reflex vasoconstriction by stimulating a sensory nerve and the fall of pressure from destroying spinal cord.

(*b*) Circulation in mammals: showing effect of bleeding and transfusion on blood pressure. Effect of chloroform and ether respectively on the circulation and respiration; influence of artificial respiration after respiration stops.

The effect of stimulating the great splanchnic in the dog before and after cutting the vagi; stimulation of the (*a*) central and (*b*) peripheral ends of the cut splanchnic.

Stimulation of the depressor nerve before and after section of the vagi (rabbit).

Effect of adrenal extract, of peptone, of cutting spinal cord high up, Traube-Hering curves, etc.

(*c*) Respiration: effect of inflation and collapse of the lung on respiratory activity; apnea; stimulating a sensory nerve; stimulating the trigeminus and superior laryngeal (causing inhibition); stimulation of the vagi with feeble and strong currents; effect of section of vagi on the frequency and depth of respiration, etc.

(*d*) Muscle and nerve experiments: showing myogram with drum at fast speed and tuning fork waves making hundredths of a second; extensibility and elastictiy of muscle; effect of heat and cold on myogram; heat rigor; effect of load on myogram; influence of veratria and suprarenal extract on muscle twitch; analysis of tetanus, showing tracings with 8, 16, 24, 40 and 50 stimuli per second; fatigue curves; electrotonus—effect of galvanic current on the irritability and conductivity of nerve, etc.

The foregoing is sufficient to acquaint the reader with the fact that physiology as taught at the State University of Texas is abreast of the leading institutions of the country and keeping pace with the commercial progress of the "New South."

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL: WINFIELD S. HALL.

No. 316. Frog-Board Myograph.—An inexpensive and convenient myograph, an improved ergograph, especially adapted to work in general physiology and pharmacology. Its advantages over other similar instruments are: 1. The muscle-nerve preparation can be made in at most one-fourth the time required for the classic preparation. 2. The muscle and nerve are not exposed to atmospheric changes. 3. The circulation of the tissues is not disturbed. This has the advantage (*a*) of permitting the study of the action of drugs on muscle tissue under normal conditions, (*b*) of studying fatigue without the accumulation of fatigue products under abnormal conditions.

No. 317. Manometer Tambour.—A modification of the classic manometer apparatus. A small tambour was joined to the distal end of the manometer by a piece of pressure tubing and supplied with a delicate tracing lever, capable of magnifying the movements of the membrane ten to twenty times, as desired. With the surface of the tambour not larger than 15 mm. and the mercury meniscus not less than 3 mm. in diameter, the most beautiful arterial pressure tracing can be obtained, showing not only the respiratory and percussion waves, but the dicrotic wave clearly superimposed on each cardiac wave.

MEDICAL DEPARTMENT, UNIVERSITY OF INDIANAPOLIS: FRANK B. WYNN AND JOHN S. WRIGHT.

Research Group.

No. 318. Banana Shreds of Fibrovascular Tissue, passed in stool and supposed to be parasites. This was reported to the Indianapolis Medical Society in 1901 by F. B. Wynn, and is the third such submitted to him for identification.

No. 319. Segments of Cabbage, probably served as slaw, passed in the stool, and supposed to be tapeworm. The resemblance to segments of the tapeworm was striking, but the microscope easily revealed the vegetable nature of the product.

No. 320. Ribbons and Shreds of Paper Passed in Stool.—Some portions resembling the segments of tapeworm; others were like the mucous casts occurring in mucous colitis. The woody fiber of many papers makes them very indigestible. They may be so intimately adherent to such things as meat, caramel candy, etc., as to escape notice, and in the stool might easily give rise to error in diagnosis.

No. 321. Fusiform Masses of Parenchyma Cells of the Lemon, passed in the stool and mistaken for parasites. The resemblance to the fluke is striking.

The foregoing specimens led to an experimental study by ten students of the university designed to show the following:

(*a*) The histology of common fruits and vegetables used as articles of diet, including apple, peach, pineapple, pear, banana, gooseberry, currant, rhubarb, grape, tomato, string bean, navy bean, onion, sugar corn, pop corn, celery, Irish and sweet potato, peanut, cabbage, kale and cucumber.

(*b*) Effect of the ordinary methods of preparing food for table use in causing disintegration. In an assigned article the student made fresh mounts from the food as found on the table at the restaurant.

(*c*) Effect of digestive processes on these foodstuffs and the recognition of partially altered food remnants which might be mistaken for parasites. Each student ate freely of an assigned article at different times, afterward searching the stools for remanants of the food taken.

These studies demonstrated very clearly that the fibrovascular tissue, especially of pineapple, rhubarb and celery, often resists the action both of cooking and the digestive juices, appearing as slender white threads in the stools, which might easily be mistaken for worms.

Nos. 322-376. Drawings and Gross Specimens Illustrative of the Foregoing.

Miscellaneous Group.

Nos. 377-382. Pulmonary Tuberculosis, Different Types.
Nos. 383-388. Liver Series.
Nos. 389-394. Kidney Series.
Nos. 395-405. Embryologic Series.
Nos. 406-411. Miscellaneous Specimens.

These were all Kaiserling preparations mounted in glycerin jelly by students of the university. The mounting was unique and artistic. The containers were Petri dishes set in heavy oak boards, which are convenient for class demonstration, non-breakable and may be stacked in drawers away from the light—a factor of importance in preserving the colors.

RUSH MEDICAL COLLEGE: E. R. LE COUNT.

Experimental Group.

Nos. 412-415. Series of Preparations Illustrating Experimental Fat Necrosis, as obtained by injecting either commercial pancreatins or extracts of fresh hog pancreas into the abdominal cavity of dogs and cats. The specimens showed the results respectively twenty-five hours, forty-eight hours, five days and nine days after injection. (See article by Wells, *Journal Medical Research,* 1903, iv, 70.)

No. 416. Gangrenous Pancreatitis with Disseminated Fat Necrosis.—This specimen was shown for purposes of comparison with the experimental lesions. The foci of fat necrosis were visible over the mesentery and omentum. At the necropsy the head of the pancreas was found to be of normal firmness, with distinct lobular markings on the cut surface and gray with reddish mottling foci. Necrosis of the entire body of the pancreas had taken place.

No. 417. Subacute Hemorrhagic Pancreatitis, with Fat Necrosis.—Specimen from a man who died of lobar pneumonia. Dark red areas, irregular in outline, were seen externally in the fresh specimen; also yellow areas. Histologic examination showed an acute inflammation in addition to extensive necrosis and hemorrhage.

Group of Heart Specimens.

Nos. 418-423. Series of Cardiac Anomalies.—These included asymmetrical pulmonary segments; fenestrated foramen ovale; perforate ventricular septum, and a rare congenital mal-development in which there was communication between the aorta and left ventricle under the base of the anterior aortic valve. Hektoen could find no mention of a similar case in literature.

Nos. 424-435. Series of Endocardial Heart Lesions.—Three of these were of acute aortic endocarditis; three of acute mitral or parietal endocarditis, and six were chronic valvular deformities resulting from fibrosis or calcareous infiltration, causing stenosis or insufficiency.

Group of Miscellaneous Specimens.

No. 436. Skeleton of a Short-Limbed Dwarf.—From a man 45 years of age. There was a fibroid thyroid, containing no demonstrable thyroidin(?). The cranial vault possesses 172 wormian bones. The skeleton has some features of osteogenesis imperfecta and some of chondrodystrophia fetalis. The absence of a clinical record and the disuse incident to deformity, with resulting alterations of the bones, are factors which make classification difficult.

No. 437. Acute Yellow Atrophy.—The hepatic tissue illustrating this rare disease was from a woman 35 years of age. She had jaundice in August, and when admitted to the hospital the following November the icterus was very deep and she had been semi-stuperous for several days. Death occurred twenty-four hours after admission. Only partial examination was permitted. In the specimen large reddish areas were noted which contained very little liver tissue; greenish districts still showed some lobular markings.

Nos. 438-439. Rupture of Spleen.—In one of these, by the passing of a wagon wheel over the body, the organ was torn in two pieces. Operation in six hours was followed in a month by complete recovery. The other was a crushing injury from an elevator. Operation in eight hours, with complete recovery. In one there was subsequent glandular enlargement.

Nos. 440-452. Miscellaneous Gross Specimens.

The instructiveness of this fine collection was greatly enhanced by very complete accompanying data—clinical and pathologic—plainly written on white paper.

JOHNS HOPKINS UNIVERSITY: HARRY T. MARSHALL AND T. S. CULLEN.

Internal Medicine Group.

These were designed to illuminate more particularly amebic dysentery, a topic prominently considered in the Section on Practice of Medicine.

Nos. 453-456. Amebic Dysentery.—These specimens showed very typically the intestinal lesions.

Nos. 457-460. Amebic Liver Abscess.

Nos. 461-464. Intestinal Lesions of Typhoid.

Nos. 465-468. Tuberculous Ulcers of the Intestine.—The typhoid and tuberculous lesions of the intestines were exhibited for purposes of differentiation from dysenteric lesions.

Gynecologic Group.

These were limited to uterine myomata and represented the cullings of material obtained at the Johns Hopkins Hospital. The specimens and drawings were used in illuminating a paper read by T. S. Cullen before the Section on Obstetrics and Diseases of Women.

No. 469. Myoma Showing Sarcomatous Nodules in Middle.

No. 470. Specimen Showing Transition of Myomatous Fibers into Sarcoma.

No. 471. Diffuse Adenomyoma, occupying inner layers of uterus and forming a complete zone around the uterine cavity. Histologic examination showed that the gland elements were derived entirely from the mucosa.

No. 472. Early Adenocarcinoma of Body Associated with Myoma.—The growth was so recent that the mucosa was not in the least thickened.

Nos. 473-478. Cervical and Submucous Myomata.

Nos. 479-496. Myomata Showing Various Degenrative Changes.

Nos. 497-568. Drawings Made from Sections of the Foregoing Tumors.

These two very complete groups of specimens were contributed in conformity with the wishes of the committee, aiming thus to illuminate subjects of prominence considered on the section programs.

MEDICAL DEPARTMENT, WASHINGTON UNIVERSITY : WILLARD BARTLETT.

Experimental Group.

Nos. 569-577. Experimental Intestinal Anastomosis.—These specimens were obtained from dogs, and are used for teaching purposes in the university. They were beautifully prepared and showed well the following:

(*a*) End-to-end anastomosis, Connell suture, 30 hours. Illustrating too long a diaphragm.

(*b*) End-to-end anastomosis, Halstead peritoneal suture, 5 days. Too long a diaphragm.

(*c*) End-to-end anastomosis, Connell suture, 16 days. Illustrating the small diaphragm which should be present at this time.

(*d*) End-to-end anastomosis, Connell suture, 40 days. Almost complete disappearance of diaphragm, and re-establishment of normal lumen.

(*e*) Lateral anastomosis, Halstead peritoneal suture, 21 days. Showing the growing together of new opening.

(*f*) Lateral anastomosis, Halstead peritoneal suture, four Connell through-and-through sutures added 21 days. Opening prevented from growing together by last-named sutures.

(*g*) Lateral anastomosis, Halstead peritoneal sutures, 28 days. Showing new opening more grown together than in (*e*).

(*h*) Lateral anastomosis, two rows of continuous Lembert sutures, one through peritoneum and other through all coats of bowel, 49 days.

(*i*) Lateral anastomosis, Halstead peritoneal suture, 87 days. Illustrating a new opening so grown together that there is distension of the proximal loop in consequence.

Miscellaneous Group.

Nos. 579-585. Miscellaneous Gross Specimens.

ST. LOUIS UNIVERSITY: WILLARD BARTLETT.

Nos. 578-585. Miscellaneous Gross Specimens.

These were all prepared by the Kaiserling method and illustrated various pathologic points well. Metastatic sarcoma was beautifully shown in the lung, liver, kidney and spleen.

COLLEGE OF PHYSICIANS AND SURGEONS, CHICAGO: W. T. ECKLEY.

Nos. 596-621. Anatomic Specimens.

Nos. 622-633. Gross Pathologic Specimens.

The first set was beautifully prepared, semi-moist specimens used by the exhibitor in teaching in the college. Accompanying these was a batch of theses by students, containing a large number of original drawings, testifying forcefully to the excellent work done in the institution in this department. This is the third successive year in which this institution has contributed ably toward the Scientific Exhibit of the Association.

ST. PETER STATE HOSPITAL, MINNESOTA: H. D. VALIN.

Nos. 634-648. Casts of Pathologic Brains.—Illustrating the following pathologic conditions: Porencephaly, glioma, amniotic adhesion band, destruction of cortex, localized internal hydrocephalus and hematoma duræ. (Made in the laboratories of the institution.)

Nos. 649-658. Surface Anomalies of Convolutions and Sulci.

Nos. 659-664. Anatomic Casts of Brain and Cord.

Nos. 665-779. Album of Photomicrographs.—The first sixteen were of the brain cortex of the cat and rat, showing, by way of comparison, sections before and after the various stages of fatigue. The remainder were of various pathologic conditions of the central nervous system, including acute delirium; first, second and last stages of degeneration in cells; capillary hemorrhages into the brain cortex; asphyxia in epilepsy; multiple embolism (luetic); hemiatrophy and hemisoftening, diseased and healthy sides; atrophy of auditory cortical center compared with opposite side; senile and mania-dementia, with degeneration of cortex; sclerosis of comma tract in general paresis; tumor of pituitary; glioma; tumor of spinal cord, and many others.

Nos. 780-815. Lantern Slides of the Foregoing.

The photomicrographs were artistic in showing the utmost detail of histologic structure and were made doubly interesting by the very complete and methodical, clinical and pathologic data which accompanied them.

COOK COUNTY HOSPITAL, CHICAGO: F. G. HARRIS.

The following collection consisted of choice Kaiserling preparations. Some were of unusual pathologic as well as clinical interest. It is creditable to the institution to have made such a contribution.

No. 816. Ileum Showing Attached Hookworms.—These specimens of *Uncinaria americana* were from a man aged 52 years who had lived in Panama for twenty-five years. For a year and a half previous to death he suffered from severe progressive anemia. The eggs and larvæ were found in the stools. Blood examination gave the following: Reds, 840,000; whites, 4,500; hemoglobin, 12 per cent.; eosinophiles, 13 per cent.; no nucleated reds. (Reported by Copps, The Journal A. M. A., January, 1903.)

No. 817. Charcot Knee Joint.—The specimen showed beautifully the destruction of the ligaments, cartilages and synovial membranes; also the erosion of the bones and periarticular fibrosis. The patient was a man who contracted syphilis fifteen years previously. For two years he noted a progressive and painless enlargement of the joint. Excessive mobility interfered with locomotion. Other symptoms and signs of tabes dorsalis present.

No. 818. Puerperal Endometritis-Infection with Bacillus Aerogenes Capsulatus.—Specimen obtained from a woman 24 years of age, confined three days before death. Gas containing cavities were to be seen throughout the uterus.

No. 819. Myeloma of Femur.—Circumference of knee, 28 inches. Tumor transparent to *x*-rays. The patient, a woman of 30, received an injury to the knee seven years ago. Six months later progressive enlargement of the knee began and was accompanied by some pain and limitation of motion. No metastases.

No. 820. Congenital Cystic Kidney.

No. 821. Bilateral Cystic Kidneys.

No. 822. Unresolved Pneumonia.

No. 823. Aneurism of Thoracic Aorta.

No. 824. Aneurism of Abdominal Aorta.

No. 825. False Aneurism of Abdominal Aorta.

No. 826. Serofibrinous Pericarditis.

No. 827. Adhesive Pericarditis.

No. 828. Atrophic Cirrhosis of Liver.

No. 829. Metastatic Carcinoma Lungs.

No. 830. Metastatic Carcinoma Liver.

No. 831. Splenic Cyst.

No. 832. Interstitial Carcinoma Stomach.

The following series of specimens was entirely in illustration of the gross lesions of malaria.

U. S. ARMY MEDICAL MUSEUM, WASHINGTON, D. C.: COL. CALVIN DE WITT.

No. 833. Spleen and Kidney in Chronic Malarial Poisoning.

No. 834. Darkly Congested Kidney, Pernicious Malarial Fever.—Estivo-autumnal parasite found in spleen. H. E. N., aged 23, white. Admitted March 2, 1900, to Post Hospital, Cebu, Philippine Islands; April 15 was outdoors and exposed to sun; fainted, and blood appeared in urine and feces. On the 18th and 19th there was much restlessness and prostration; unconsciousness; intense yellowishness of skin and conjunctiva; persistent vomiting; involuntary urination and defecation; heart action weak; constantly under strychnia stimulation. Repeated peripheral examination of blood failed to show malarial parasite. Urine blackish and contained vast numbers of partly disintegrated blood corpuscles and blood casts; little albumin; no epithelium or casts; color much improved during last twenty hours of life. Died 19th. Necropsy three hours after death. Lungs apparently normal; liver a muddy color; gall bladder contained a thick, tarry bile; small intestine much stained with bile and contained twelve lumbricoid worms; kidneys darkly congested; spleen much enlarged, dark and congested; scrapings from latter showed microscopically the estivo-autumnal parasites, containing large pigment granules in active motion.

Nos. 835-836. Spleen and Kidney in Pernicious Malarial Fever.—From the Philippines.

No. 837. Spleen in Chronic Malaria.—From the Philippines.

This special series was solicited by the Committee. It makes the second time that the Army Medical Museum has contributed liberally, under the direction of Col. DeWitt, to the Scientific Exhibit of the Association.

The Indiana State Medical Association was the first organization to institute the scientific exhibit as a feature of society work, and to its efforts may be attributed the introduction of the exhibit into the American Medical Association. The collection was entirely of dry specimens.

INDIANA STATE MEDICAL ASSOCIATION: FRANK B. WYNN.

No. 838. Skull Trephined by Baron Larrey, surgeon of Napoleon I. During the retreat from Moscow in 1812 the man was cut down by a Russian cossack and left on the field twenty-four hours. He recovered after trephining, and continued in the service a year. Died in 1873. Just above the squamous portion of the temporal is a quarter-sized opening in the calvarium, where the button was removed, and extending two inches from it the evidence of a saber cut. He suffered slight difficulty in speech. (Fletcher.)

No. 839. Enormous Distension of Colon from Retained Feces.—This specimen was obtained by Drs. Gieb and Jones, Groton, S. D., from G. K., who went for one year and three days without a bowel movement. For the first six months he ate three hearty meals a day, doing harvest work. Later he could only do light work. At some points the bowels measured 19¼ inches.

Nos. 840-879. Collection of Vesical Calculi.—This fine series of stones was obtained by operations, during a residence of eleven years in Persia, by J. G. Wishard. Some of the cases were operated on under the most trying circumstances, in filthy and crowded quarters, and in some instances in stables.

No. 880. Ten Renal Calculi.—Product of one nephrectomy; weighing 5 ounces. The patient was a man, 39 years of age. Several years previously he had been injured by the caving in of a pit. Had hematuria for a week, but no further renal symptoms. For a year and a half previous to the operation by F. R. Charlton he had been treated for stomach trouble, persistent vomiting being the most conspicuous symptom. At the time of operation there was tenderness over the back and pus in the urine. Nephrotomy was first performed, a pint and a half of pus and the stones were removed; ten days later the kidney was removed. Recovery.

No. 881. Epidermal Cast of Foot.—Hemorrhagic smallpox. (Brayton.)

Nos. 882-902. Miscellaneous Specimens.—Including enteroliths, hair balls, foreign bodies removed from the larynx by operation, etc.

GEORGE E. SHAMBAUGH, CHICAGO (PRIVATE COLLECTION).

Nos. 903-906. Series of Wood's Metal Casts of Ear.—1. Two casts of labyrinth mounted on stiff cardboard, with drawings of anterior and posterior surfaces. 2. Metal cast of ear showing: (*a*) Meatus auditorius externus; (*b*) cellulæ mastoidæ; (*c*) meatus acousticus internus; (*d*) the osseus labyrinth. 3. Cast same as No. 2 and showing, in addition, the aquaductus vestibuli and the canaliculus cochleæ, with its accessory canal for the exit of the large vein from the cochlea.

Nos. 907-918. Series of Celloiding Casts of Labyrinth, mounted in cells and made from a preparation in which the blood vessels had been previously injected. 1. Complete cast of labyrinth, showing a perfect injection of the capillaries as well as the arteries and veins. Two drawings of the preparation in colors. 2. Cast of the cochlea, showing the arterial tree alone. Drawing of same in colors. 3. Drawings in colors to show following: (*a*) Basal coil of cochlea of embroyos 11 cm. long; (*b*) venous tree of cochlea; (*c*) basal coil of cochlea of fetus, full term; (*d*) cross section of cochlea; (*e*) detail of piece from basal coil of cochlea; (*f*) semicircular canal with ampulla; (*g*) detail drawing of section of the semicircular canal.

R. W. GILLMAN, DETROIT (PRIVATE COLLECTION).

Nos. 919-937. Series of Temporal Bones.—Arranged in order to show the varying distance of the lateral sinus from the spina sup. meatus. In No. 1 the distance was 21.0 mm. In each succeeding specimen the sinus was shown nearer the meatus, and in No. 17 they were only 6.0 mm. apart.

EDWARD EVANS, LA CROSSE, WIS. (PRIVATE COLLECTION).

Nos. 936-947. Products of Twelve Cholecystotomies.

Nos. 948-953. Appendiceal Specimens.

The stones in each cholecystotomy case were beautifully mounted on a board. The essential points of interest to the appendiceal specimens were the foreign bodies found in the appendix. In one case there was an apple seed; in another two live round worms were found in an abscess surrounding the perforated appendix.

The following exhibit was a beautiful series of casts of the bladder and prostate gland, designed to show the different types of hypertrophy of the latter, with the view of illustrating the particular form of surgical treatment indicated in each case.

BRANSFORD LEWIS, ST. LOUIS (PRIVATE COLLECTION).

No. 954. Bilateral Enlargement, with obstruction from pedunculated intravesical growth. Suprapubic operation advisable.

No. 955. Moderate Enlargement of Lateral Lobes; thick prostatic bar; deep bas fond; marked curvature of urethra. Favorable for perineal prostatectomy.

No. 956. Enlargement of Both Lateral Lobes; pedunculated median intravesical tumor from posterior commissure. Suitable for suprapubic removal.

No. 957. Pedunculated Median Intravesical Growth from posterior commissure. Favorable for suprapubic removal.

No. 958. Excessive Enlargement of Lateral and Median Lobes; direct pressure on both ureter openings producing dilatation of ureters and renal pelves. Favorable for combined suprapubic and perineal removal.

No. 959. Lateral Lobes, Enlarged; especially right; high prostatic bar, with small nodule on right; deep bas fond. Favorable for Bottini or perineal prostatectomy.

No. 960. Marked Enlargement of Both Lateral Lobes, and globular intravesical tumor from posterior commissure. Removal of tumor and both lobes required; best accomplished through perineal and possibly suprapubic combined routes. Bottini inappropriate.

No. 961. Moderate Enlargement of Lateral Lobes.—Pyramidal median projection capable of ball and socket effect. Suitable for suprapubic removal.

No. 962. Multiple Adenomata projecting into prostatic urethra. Favorable for perineal removal. Bottini inappropriate and inadequate.

HERMAN TUHOLSKE, ST. LOUIS (PRIVATE COLLECTION).

No. 963. Placenta Attached to Liver.

This remarkable specimen is the only one of its kind reported. The nearly full term fetus was removed from the abdomen by operation, but the woman died a few hours later from secondary hemorrhage.

H. F. HARRIS, ATLANTA (PRIVATE COLLECTION).

Nos. 964-966. Malarial Plasmodium.—Preparations stained by the modified Romanowsky process.

No. 967. Ameba from case of amebic dysentery in man.

No. 968. Ameba from a case of dysentery experimentally induced in a dog.

CLAUDE A. SMITH, ATLANTA, GA. (PRIVATE COLLECTION).

No. 969. Gross Specimens of Uncinaria americana.

Nos. 970-972. Microscopic Mounts, showing both the hookworm and ova.

MIHRAN K. KASSABIAN, PHILADELPHIA (PRIVATE COLLECTION).

Nos. 973-1012. Collection of Skiagraphs.

These skiagraphs were excellent. The more noteworthy among them were: (*a*) Pleurisy with effusion. (*b*) Vesical calculus. (*c*) Congenital dislocation of both hips (reduced by Lorenz).

W. C. FUCHS, CHICAGO (PRIVATE COLLECTION).

Nos. 1013-1113. Radiographs.—Rare in this collection were the following: (*a*) Four-month fetus differentiated from tumor; (*b*) pus sac-recurrent appendicitis; (*c*) floating kidney; (*d*) pericarditis; (*e*) gallstones; (*f*) cyst of the brain.

EXECUTIVE SESSION

Tuesday, May 5—Afternoon.

Called to order at 2:30 p. m.

Address by the Chairman, Victor C. Vaughan of Ann Arbor, Mich.

Abstract of Papers 1 to 8, being contributions from the Hygienic Laboratory of the University of Michigan, reported by Victor C. Vaughan, director.

(1) "The Chemistry of the Bacillus Coli Communis," by Mary F. Leach, Ann Arbor.

(2) "The Chemistry of the Bacillus Typhosus," by May Wheeler, Ann Arbor.

(3) "The Toxicity of the Intracellular Substance of Bacillus Typhosus," by Louis M. Gelston, Ann Arbor.

(4) "The Anthrax Toxin," J. Walter Vaughan, Ann Arbor.

(5) "The Intracellular Toxin of Bacillus Pyocyaneus," by Daniel McIntyre, Ann Arbor.

(6) "A Preliminary Chemical Study of the Hepatic Cells of the Ox," Frank Spencer and Frederick Munson, Ann Arbor.

(7) "The Toxicogenic Bacteria Found in Drinking-Water," William G. Carhart, Ann Arbor.

(8) "The Chemical Tests for Morphin in the Presence of the Products of Bacterial Decomposition," by Myron W. Clift, Ann Arbor.

Discussion on the above by Henry A. Christian, Boston; A. C. Croftan, Chicago; W. S. Carter, Galveston; Joseph McFarland, Philadelphia.

The Secretary made announcement of the banquet.

Paper by Walter L. Bierring, Iowa City, Iowa: "Multiple Periosteal Sarcomata of the Cranium, with Involvement of Retroperitoneal Lymph Nodes and Attending Severe Anemia.

Appointment of Nominating Committee: E. R. LeCount, Chicago; W. L. Bierring, Iowa City; Frank B. Wynn, Indianapolis.

Discussion of Dr. Bierring's paper by E. R. LeCount, Chicago, and Henry A. Christian, Boston.

Wednesday, May 6—Morning.

Paper by E. A. de Schweinitz, Washington, D. C., read by Joseph McFarland, Philadelphia. Discussed by Walter B. Dorsett, Washington, D. C.; L. Hektoen, Chicago; Victor C. Vaughan, Ann Arbor; Joseph McFarland, Philadelphia.

Paper by Joseph McFarland, Philadelphia: "Studies of Antivenene." Discussed by L. Hektoen, Chicago; J. W. Foss, Phœnix, Ariz.

Paper by W. S. Carter, Galveston, Tex.: "The Protoplasmic Activity of the Renal Epithelium as Determined by the Elimination of Pigments Injected into the Circulation." Discussed by E. R. LeCount, Chicago.

Paper by L. W. Dean, Iowa City, Iowa: "The Influence of Consanguinity on the Organs of Special Sense, Especially on the Organs of Vision." Discussed by J. W. Foss, Phœnix, Ariz.

Paper by J. W. Foss, Phœnix, Ariz.: "Streptococcic Infection of the Lungs Successfully Treated by Antistreptococcic Serum." Discussed by Guido Bell, Indianapolis; H. N. Graves, Georgetown, Tex.; W. S. Carter, Galveston; Louis Leroy, Nashville, Tenn.

Nominating Committee reported as follows: Chairman, Joseph McFarland, Philadelphia; secretary, Henry T. Christian, Boston; delegate, A. P. Ohlmacher, Gallipolis, Ohio, all of whom were elected.

WEDNESDAY, MAY 6—AFTERNOON.

Paper by J. M. Frazier, Belton, Tex. Discussed by H. B. Ward, Lincoln, Neb.

Paper by Henry B. Ward, Lincoln, Neb.: "Precision in the Determination of Human Parasites." Discussed by Frank B. Wynn, Indianapolis; W. L. Bierring, Iowa City; Allen J. Smith, Galveston, Tex.

Paper by Thomas S. Cullen, Baltimore, Md.: "Condition of the Endometrium in Case of Uterine Myomata." No discussion.

Paper by Louis Leroy, Nashville, Tenn.: "A Case of Aerogenes Capsulatus Infection of the Neck." Discussed by L. Hektoen, Chicago.

Paper by Henry A. Christian, Boston: "The Neuroglia and the Ependymal Epithelium of Teratoid Tumors." Discussed by L. Hektoen.

Paper by L. Hektoen, Chicago: "A Case of Short-Limbed Dwarfism," illustrated with lantern slides.

Paper by E. R. LeCount, Chicago, in the name of Peter Bassoe, Chicago: "A Case of Gigantism and Leontiasis Ossea," with lantern demonstration.

Paper by F. G. Novy and W. J. McNeal, Ann Arbor: "The Cultivation of Trypanosoma Lewisii." Discussed by H. B. Ward, Lincoln, Neb.

Adjourned, after vote of thanks to the retiring officers.

THURSDAY, MAY 7—AFTERNOON.

Paper by Newton Evans and F. J. Otis, Battle Creek, Mich.: "The Morphology and Biology of the Parasites of Blastomycetic Dermatitis," with lantern demonstration. No discussion.

Paper by Claude A. Smith, Atlanta, Ga.: "Further Observations of Ankylostomiasis in the South." Discussed by H. B. Ward, Lincoln, Neb.

Paper by Henry B. Ward, Lincoln, Neb., on "Some Points in the Development of Dermatobia Hominis."

Paper by J. G. Holmes, Chicago, read by W. S. Hall, Chicago: "The Working Capacity of a Muscle." Discussed by Henry Sewall, Denver.

Demonstration of new physiologic apparatus. Winfield S. Hall, Chicago.

On motion the following papers were read by title:

W. S. Newcomet, Philadelphia: "Tissue Changes under X-Ray Influence."

F. Robert Zeit, Chicago: "Endothelioma of the Uterus."

Final adjournment.

INDEX

Aerogenes capsulatus infection of neck, case of, 79
Bierring, W. L., discussion on cranial sarcomata, 16
Bierring, W. L., discussion on human parasite, 74
Bierring, W. L., multiple periosteal sarcomata of cranium, 9
Blastomycosis, systemic, morphology and biology of parasite in case of, 110
Capacity of human muscle for work, the, 150
Carter, W. S., discussion on protoplasmic activity of renal epithelium, 50
Carter, W. S., protoplasmic activity of renal epithelium, 35
Christian, H. A., discussion on cranial sarcomata, 15
Christian, H. A., discussion on teratoid tumors, 109
Christian, H. A., teratoid tumors, 87
Consanguinity, influence of, on organs of special sense, 51
Contents, 7
Cranium, multiple periosteal sarcomata of, 9
Cullen, T. S., condition of endometrium in uterine myomata, 77
Dean, L. W., influence of consanguinity on organs of special sense, 51
De Schweinitz, E. A., apparent immunizing value of attenuated tubercle bacilli, 17
Discussion on aerogenes capsulatus infection, 86
Discussion on consanguinity and organs of special sense, 57
Discussion on cranial sarcomata, 15
Discussion on human parasite, 72
Discussion on immunizing by attenuated tubercle bacilli, 22
Discussion on protoplasmic activity of renal epithelium, 50
Discussion on rennet and antirenene, 34
Discussion on teratoid tumors, 109
Discussion on uncinariasis, 148
Dorsett, M., discussion on immunization by attenuated tubercle bacilli, 22
Endometrium in uterine myomata, 77
Evans, N., parasite of systemic blastomycosis, 110
Executive Session, 188
Foss, J. W., discussion on consanguinity, 57
Foss, J. W., discussion on rennet and antirenene, 34
Frog-board myograph, 167
Hall, W. S., new physiologic apparatus, 167
Hektoen, L., discussion on aerogenes capsulatus infection, 86
Hektoen, L., discussion on immunization by attenuated tubercle bacilli, 22
Hektoen, L., discussion on rennet and antirenene, 34
Hektoen, L., discussion on teratoid tumors, 109
Holmes, J. G., capacity of human muscle for work, 150
Human muscle, capacity of, for work, 150
Human parasite, precision in the determination of, 58

Immunity tests on cattle, 19
Immunizing value of attenuated tubercle bacilli, apparent, 17
LeCount, E. R., discussion on cranial sarcomata, 15
LeCount, E. R., discussion on protoplasmic activity of renal epithelium, 50
Leroy, L., case of aerogenes capsulatus infection of neck, 79
Leroy, L., discussion on aerogenes capsulatus infection, 86
McFarland, J., discussion on immunization by attenuated tubercle bacilli, 22
McFarland, J., discussion on rennet and antirenene, 34
McFarland, J., rennet and antirenene, 24
Manometer tambour, the, 170
Morphology and biology of the parasite from case of systemic blastomycosis, 110
Myomata, uterine, condition of endometrium in cases of, 77
Neuroglia tissue and ependymal epithelium in teratoid tumors, 87
Officers, 5
Otis, F. J., parasite of systemic blastomycosis, 110
Physiologic apparatus, new, 167
Protoplasmic activity of renal epithelium, 35
Renal epithelium, protoplasmic activity of, 35
Rennet and antirenene, experiments with, 24
Sarcomata, multiple periosteal, of cranium, 9
Scientific exhibit, report on, 174
Smith, A. J., discussion on human parasite, 74
Smith, C. A., discussion on uncinariasis, 149
Smith, C. A., uncinariasis in the South, 135
Teratoid tumors, neuroglia tissues and ependymal epithelium in, 87
Tubercle bacilli, apparent immunizing value of attenuated, 17
Uncinariasis in the South, 135
Vaughan, V. C., discussion on immunization by attenuated tubercle bacilli, 23
Ward, H. B., discussion on human parasite, 75
Ward, H. B., discussion on uncinariasis, 148
Ward, H. B., precision in determination of human parasite, 58
Wynn, F. B., discussion on human parasite, 72

WELLCOME LIBRARY INSTITUTE